RICKETS

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RICKETS

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РАХИТ

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PREFACE

Rickets was known as far back as early antiquity. Soranus of Ephesus (early 2nd century A.D.) described leg and spinal deformities in children. Galen (130-201 A.D.) described rachitic changes in the osseous system, including thoracic deformities, in greater detail.

In the 15th century this disease was quite widespread, especially in the large towns of North Europe. The Danish and Dutch painters of the time not infrequently portrayed children with thickened epiphyses, deformed chests, olympian foreheads, etc.

In the 17th century the children of England were widely affected with rickets. Descriptions of severe forms of this disease began to appear with increasing frequence in the works of English physicians and this fact warranted calling rickets the "English disease". The first work on the clinical aspects and anatomy of rickets, exhaustive for the time, belongs to the pen of Francis Glisson, English physician (1650). By the beginning of the 19th century the clinical picture of rickets was already very well known.

Russian authors have made a great contribution to the study of this disease. In his *Pediatrics*, published in St. Petersburg in 1847, S. F. Khotovitsky not only described in detail the skeletal changes, but also indicated such concomitant symptoms of rickets as hidrosis, muscular flaccidity, retarded motor development, changes in the gastrointestinal tract, etc. At the same time he noted

that an abundance of farinaceous and sweet foods, limited physical exercise, insufficient sunlight and fresh air, as well as debilitating diseases, were factors greatly conducive to development of rickets.

In his dissertation "On the Question of the Pathogenesis of the English Disease" N. S. Korsakov (1883) had established the importance of calcium in the pathology of this disease long before any chemical studies of the mineral metabolism in rachitic children were made. A. A. Kisel wrote his dissertation on the pathoanatomical changes in the bones of growing animals under the influence of minimal doses of phosphorus. V. P. Zhukovsky's dissertation (1894) was a result of his studies of the development of the "English disease" ("rachitism and rachitic deformities") among the children of St. Petersburg's workers.

I. A. Shabad's monograph *Calcium in the Pathology of Rickets* (1909) is still of considerable interest as the first study of mineral metabolism. M. S. Maslov in his dissertation "On the Physiological Importance of Phosphorus for the Growing Organism" (1913) revealed the deep metabolic processes in the child's organism.

A considerable contribution to the studies of the etiology, pathogenesis and clinical aspects of rickets has been made since the Great October Socialist Revolution by Russian pediatricians. Methods of prophylaxis and treatment have been elaborated in the works of Y. M. Lepsky, M. S. Maslov, A. F. Tur, Y. F. Dombrovskaya, P. S. Medovikov, S. O. Dulitsky, I. V. Tsimbler and the workers of the clinics under their supervision.

The works published since the last war deal with special clinical aspects, course and treatment of rickets in the unfavourable external environment produced by the war.

Rickets was formerly believed to be a disease of the moderate zone of Europe and America, the central cold belts and highly humid areas. But this view is incorrect. Rickets occurs both in countries located in the middle

latitudes and in the cold North and the hot South. Depending on the character of feeding, the child's general regimen and external environment (in the broad sense of the word), the difference may consist in the extent to which the disease is spread, as well as the forms and severity of its manifestations.

Rickets is quite widespread in many countries. At the end of last century examination of children of the East End of London, inhabited mainly by workers' families, revealed rickets in 80 per cent of the cases. In 1915 symptoms of rickets were observed in almost 80 per cent of the English primary school pupils. According to official figures of the British Ministry of Health, 87 per cent of kindergarten children suffered from rickets in 1928. In the city of Sheffield (England) 78.8 per cent of the children between 3 and 6 months of age were affected with this disease in 1944.

In 1930-33 rickets was found in 49.8 per cent of white children and 87.7 per cent of Negro children in the State of Tennessee (U.S.A.) In 1937 this disease was observed in 91-98 per cent of pre-school children in some large American cities.

In the 1940's rickets was observed in 74.2 per cent of the children between 2 and 3 years of age living in the industrial cities of Germany. In Belgium 80-90 per cent of the children were affected with rickets. A similar or somewhat lower rickets incidence was observed in other countries (A. N. Antonov, S. O. Dulitsky, Y. M. Lepsky).

The incidence of rickets among children in tsarist Russia was extraordinarily high. In large industrial cities this disease affected almost all children, 80 per cent of them suffering from rickets in Moscow (A. A. Kisel) and 95 per cent in Petersburg (V. P. Zhukovsky).

After the Great October Socialist Revolution the incidence of severe forms of rickets diminished, although the disease continued to be considerably widespread.

Of the total number of children under observation of

infant health centres in 1927, 57.6 per cent had rickets in Moscow, 69-82 per cent in Leningrad (according to individual infant health centres) and 64.9 per cent in Odessa (Y. M. Lepsky). Examination of children between 2 months and 2 years of age in Baku in 1939 revealed symptoms of rickets in 62.3 per cent of the cases (S. I. Gajiyeva). By 1949 the number of rachitic children considerably diminished and the grave forms leaving skeletal deformities disappeared.

In the Soviet Union the unfavourable living conditions engendered by the war raised the incidence of rickets not only among infants, but also among pre-school and school children. The number of children with second and third degree rickets more than doubled.

Since the end of the last war the steady rise in material and cultural standards of the population, the child protection measures and the increasingly more effective methods of preventing and treating various diseases since the end of the last war have led to a sharp reduction in child morbidity and mortality in the Soviet Union. The incidence of rickets among children has diminished and its severe forms have become a rare occurrence.

Nevertheless, clinical aspects, treatment and prevention of rickets are still urgent questions, since this disease continues to play a big part in child pathology.

It can no longer be doubted that rickets is a factor that diminishes the reactivity and immunobiological properties of the child's organism, increases its susceptibility to various diseases and, consequently, leads to greater morbidity and mortality. It should be noted that the resistance of the child's organism to various diseases is lowered not only by grave and clearly marked forms of rickets, but not infrequently also by effaced forms with barely perceptible clinical symptoms.

N. F. Filatov attached enormous importance to rickets as one of the causes of high child mortality. In his letter to S. P. Botkin in 1888 he wrote: "I am inclined to be-

lieve that children who die in the second year of life and later almost all have or had rickets and it is therefore no less important to eliminate the causes of rickets than it is to control diarrhea in children" (*International Clinic*, 1888, No. 5, p. 319).

Unfortunately, not all medical practitioners take into account this great pathological effect produced on the child's organism by rickets. G. N. Speransky is undoubtedly right in saying that "although pediatricians have efficient ways and means of preventing and treating severe forms of rickets at their disposal, they are not doing enough to prevent this disease. Some physicians fail to eliminate the harmful influence of this disease on the organism of the growing child" when they administer vitamins or expose children to irradiation indiscriminately or unsystematically, and overlook the importance of mild and effaced forms of rickets (*Medical News*, 1953, p. 1).

The Soviet health services are striving to eradicate rickets. Elimination of this disease is an indication of rational feeding, good regimen and proper care of children.

Numerous facts extending our knowledge of the etiology, pathogenesis, clinical aspects and methods of preventing and treating rickets have been accumulated in recent years. The last monograph dealing with these questions, *Rickets and Tetany of Rachitics*, was written by Y. M. Lepsky in 1941 and was republished in 1945. The author of this book has undertaken to generalise the available literary data and describe her long observations and studies. If this monograph in any way adds to the existing knowledge of the pathogenesis, clinical aspects, prevention and treatment of rickets, and helps the medical practitioners to control this disease, which is so very harmful to the organism of the child, the author will consider her aim in some measure achieved.

ETIOLOGY

It has long been known that unhygienic conditions are conducive to rickets. In children living in dark, crowded houses and spending very little time outdoors and in the sun rickets develops sooner and runs a severer course. In countries located closer to the equator, where children stay naked outdoors all day long, the rickets incidence is much lower than it is in countries with a moderate and cold climate. Rickets is also observed less frequently in children of some of the nomadic peoples. However, examinations of children of Buryat nomads in 1931 showed 85 per cent to have rickets despite the fact that they could stay out in the fresh air and sunlight all they wanted (Y. Y. Granat and Y. Zgorzhelskaya). The reason for it is that, according to a Buryat custom, the children were not taken outside their dark tents until the second year of life.

Rickets can also be observed in children living in southern countries if they are deprived of fresh air and sunlight. Even high living standards do not prevent the disease if a proper regimen is not observed. In cases of indoor life rickets affects children living even in highlands (M. Kh. Ugrelidze), where, as is well known, there is intense ultraviolet radiation.

In 1919 Huldschinsky discovered the effective action of the mercury vapour lamp (artificial mountain sunlight) in the treatment of rachitic children. Since then insufficient

irradiation of children with certain rays of the solar spectrum has been considered the main etiological factor of rickets.

Ultraviolet rays do not pass through ordinary window panes and are blocked by the air if it contains dust, soot and various vapours. Hence it is clear why rickets affects children living in lowlands with a humid climate and those living under any geographic conditions, but kept indoors during the first year of life.

The light theory also explains the seasonal character of rickets incidence.

Rickets strikes the most easily and runs the gravest course in late autumn, winter and early spring since children stay indoors for a long time, and even when outdoors they are so heavily dressed that very few ultraviolet rays penetrate to their bodies. In winter, when the sun does not rise high and the sky is long overcast with clouds, the ultraviolet rays are retained in the atmosphere and scarcely reach the earth. Fewer ultraviolet rays reach the earth's surface during early morning hours and in the evening when the sun hangs low.

The second important cause of rickets is irrational feeding of infants.

The advocates of the alimentary theory believed the development of rickets to be caused by a deficiency of calcium in the food because the bones affected with this process contain less calcium than do normal bones. The authors endeavoured to prove this experimentally by depriving experimental animals of the necessary amounts of calcium. Histological examinations have shown the bones of these animals to have defects which were not typical of rickets.

It was subsequently established that the calcium deficiency in the rachitic child's organism was not due to insufficient consumption of phosphorus and calcium with the food, but to a disturbance in the process of their assimilation by the child's organism.

It is generally recognised that breast-fed children are less frequently affected with rickets and never have severe forms of this disease. In cases of mixed and, especially, artificial feeding the incidence of rickets is much higher and the disease is severer.

The difference in the assimilation of calcium and phosphorus salts may be one of the causes of this phenomenon. A healthy breast-fed baby assimilates about 70 per cent of the calcium and 50 per cent of the phosphorus consumed with the food (Orgler); in cases of artificial feeding only 30 per cent of the calcium (I. A. Shabad) and 20-30 per cent of the phosphorus are assimilated. The calcium-phosphorus ratio (1 : 1.3-1.5) in human milk is the most favourable for the assimilation of these substances. The phosphorus and calcium of human milk are well assimilated by the child if the milk it consumes is raw. But if the child is fed drawn-off and boiled human milk, less of the phosphorus, calcium, protein fraction and fat is assimilated and more of these mineral substances and fat is excreted through the intestinal tract. This is largely due to inactivation of the enzymes, especially lipase, as a result of boiling the milk (A. B. Fridman). The vitamin C deficiency observed in children fed boiled human milk (M. N. Bessonova) in its turn sharply diminishes the enzymatic activity of the gastrointestinal tract and the acidity of the gastric juice. The alkaline reaction and deficiency of fatty acids in the upper portions of the small intestine inhibit the formation of calcium soaps, as a result of which the absorption of calcium, and, consequently, of phosphorus is disturbed.

Feeding the child boiled donor's milk is thus not equivalent to breast-feeding and does not prevent development of rickets.

But these are not the only dietary defects which lead to development of rickets. Assimilation of phosphorus and calcium requires a definite protein-fat ratio and the presence of alkaline and acid valences in the food. Prevalence

of oxalates or calcium salts over sodium may considerably affect the process of calcium absorption. Such foods as potatoes, cereals, beans and peas sharply impair assimilation of calcium. A definite ratio of calcium compounds and fat in the food (1 g of fat per 0.04-0.08 g of calcium) is necessary because a fat deficiency leads to insufficient formation of calcium salts of fatty acids (soaps). Even with adequate consumption of readily soluble calcium salts the process of their absorption in the small intestine is disturbed and leads to hypocalcemia if the amount of bile in the intestinal tract is diminished. Calcium is found in foodstuffs not only in the form of carbonates, phosphates, oxalates and fatty acid compounds, but also in an adsorbed state with proteins. It follows that assimilation of calcium also depends on protein metabolism. Normal phosphorus metabolism requires not only a definite ratio of the calcium and phosphorus compounds in the foodstuffs, but also of proteins, fats and carbohydrates, because a number of organic compounds of phosphorus with intermediate products of metabolism of these most important substances is formed in the process of assimilation. That is why a one-sided milk or carbohydrate diet of an infant, deficient in vitamins A, D, C and group B, causes a disturbance in the mineral metabolism and is conducive to the development of rickets.

Many investigators noted that children living in the Arctic Zone with no sunlight for a considerable part of the year were never or relatively rarely affected with rickets. They ascribed this circumstance to the special dietary habits of the people who consume a good deal of fish and seal flesh and fat.

In 1918 Mellanby demonstrated in an experiment with dogs that cod-liver oil acted as an anti-rachitic because it contained a special vitamin. For some time it was believed that the anti-rachitic activity of cod-liver oil depended on vitamin A already known at the time. McCollum passed a stream of oxygen through cod-liver oil,

which inactivated vitamin A, and discovered that the oil retained its anti-rachitic action. Subsequent research discovered in the nonsaponifiable part of cod-liver oil another vitamin with strong anti-rachitic action—vitamin D. It was thus definitely established that foodstuffs possess the property of preventing and curing rickets mainly in virtue of the amount of vitamin D they contain.

As a result of further research it was discovered that some foodstuffs possessing no prophylactic or curative action in rickets acquired it under the influence of ultraviolet rays. On irradiation the sterols contained in the foodstuffs (cholesterol, ergosterol) form substances some of which are members of the vitamin D group. This made it clear that irradiation of the child with short-wave ultraviolet rays formed vitamin D (D_3) in its skin, which is the essence of the anti-rachitic action of the rays of sunlight or a mercury vapour lamp. This gave rise to a firm conviction that rickets was caused by a vitamin D deficiency.

In addition to the afore-mentioned causes great importance in the etiology of rickets is also attached to other factors. According to some observations prematurely born babies are particularly susceptible to rickets. This is due not only to the increased vitamin D requirements of such children, as a result of their rapid growth and development, but also apparently to the fact that the specific injuries to the fetus, responsible for the premature birth, weaken the child's organism and in an unfavourable external environment facilitate the development of the rachitic process (M. S. Maslov).

No small part in the emergence of rickets is played by the diseases the child has survived. Gastrointestinal disorders lead to disturbance of all forms of metabolism, including that of minerals. In such cases acidosis quickly develops and there is a deficiency not only of vitamin D, but also of vitamins A, C and B, which in their turn facilitate development of rickets. A similar pathological effect is produced by respiratory diseases, all acute infectious

diseases, etc. It has been demonstrated, both experimentally and clinically, that disorders of the endocrine functions are conducive to emergence of rickets.

It was formerly held that rickets could be congenital. This was asserted in works published at the end of the 19th and the beginning of the 20th centuries (Kassowitz, Marfan, Czerny, Ploos van-Amstel, et al). The authors believed the small thickenings on the ribs at the junction of bone and cartilage or the softening of the flat bones of the skull to be manifestations of rickets in the newborn. The development of congenital rickets was associated with intrauterine diseases of the fetus (P. Giraud, Louchet) and entirely groundlessly with a hereditary predisposition.

N. F. Filatov, P. S. Medovikov, P. V. Kuskov, F. Y. Chistovich, A. Razumovsky, G. N. Speransky, A. F. Tur, M. S. Maslov and Wieland deny the existence of congenital rickets. The changes in the bones (soft skull bones, pliable sutures, negligible swelling at the bone-cartilage junction of the ribs), most frequently observed in prematurely born children, on closer scrutiny, prove to be nonrachitic but connected with incomplete physiological ossification and usually disappear by the second or third month of life.

Of interest in this respect is the work of Z. G. Korolyova (1955). By observing 712 children from the moment of their birth she discovered soft skull bones in 71 of them at the age of 2-3 weeks. In some of them one parietal bone was soft, in others—both bones, the softening affecting a narrow line along the sagittal suture or on the parietal bones parallel to the lambdoid suture. In some children the softening affected vast sections of both parietal bones. Marked changes in the parietal bones were usually observed in prematurely born children, or in those who were underweight at birth, and disappeared by the end of the fourth or fifth week. Roentgenoscopy of the shin and forearm bones revealed no deviations from the

normal structure. The phosphorus and calcium content in the blood serum was within the norm for healthy children of that age. Pathomorphological examinations of dead children, who had soft skull bones when alive, revealed no signs of rickets. These data once more disprove the existence of congenital rickets.

In conclusion it may be said that rickets is a disease conditioned mainly by social factors, for which reason it gained currency first among children of the indigent sections of the population in large industrial towns. Low material and cultural standards of the family, poor housing conditions, violation of the rules of hygiene in caring for the child, insufficient use of fresh air and sunshine and lack of regular physical exercise are all factors conducive to rickets. The character of feeding—one-sided, inadequate diet with insufficient vitamins A, D, C and B—is, as was already mentioned, particularly important. The health of the child's mother also plays a big part. The diseases suffered by the woman during pregnancy may essentially affect the child's development, weaken its organism and facilitate the subsequent emergence of rickets.

PATHOGENESIS

The pathogenesis of rickets cannot as yet be considered definitely established despite the many existing hypotheses.

One of the clearly established pathogenic factors in rickets is the disturbance of mineral metabolism. I. A Shabad was the first to show (1907-15) that the positive calcium balance decreases in the very beginning of the disease, becomes sharply negative at the height of it and positive again on recovery. He, too, discovered a change in phosphorus metabolism. It was subsequently demonstrated that the primary disturbance in the phosphorus metabolism occurs in the beginning of disease, while the calcium balance may still be positive. During convalescence the phosphorus balance is the first to improve; on complete recovery the calcium balance also becomes positive. I. A. Shabad's data were confirmed by foreign authors only several years later; today they are generally recognised. A more detailed study of the calcium and phosphorus in the blood subsequently conducted by I. A. Shabad, L. L. Begam, I. V. Tsimbler, et al, has shown that four phases of changes in phosphorus and calcium metabolism in accordance with which the $\frac{Ca}{P}$ coefficient is altered can be established during the different stages of the disease. In a healthy child the calcium-phosphorus ratio is 2 (10-11 mg% calcium and 5 mg% phosphorus).

During the first phase the amount of inorganic phosphorus in the blood decreases and that of calcium remains normal; the $\frac{Ca}{P}$ coefficient increases.

During the second phase, at the height of rickets, the amount of calcium also decreases; the $\frac{Ca}{P}$ coefficient decreases.

During the third phase (convalescence) the amount of phosphorus increases, while that of calcium remains diminished; the $\frac{Ca}{P}$ coefficient continues to decrease.

During the fourth phase (corresponding to recovery) the amounts of phosphorus and calcium become normal and the $\frac{Ca}{P}$ coefficient increases.

The overwhelming majority of rickets patients exhibit hypophosphatemia. According to the author's observations, phosphorus is definitely diminished in 83.6 per cent of the children with a clear clinical picture of rickets. An amount of calcium below 9 mg% was noted in 72 per cent of the children; of these the amount was between 8 and 6 mg% in 28 per cent.

The disturbances in calcium and phosphorus metabolism are more strongly pronounced in severe forms of rickets and at the height of the disease. Low figures of phosphorus in the blood (3.2-3.5 mg%) are found in 33 per cent of the children with second degree rickets and in 85 per cent of the children with third degree rickets. A similar correspondence is noted in the case of calcium. During convalescence the biochemical indices improve in a considerable number of children, long remaining diminished in other children.

The changes in the phosphorus and calcium content depend not only on the severity and period of the rachitic process, but also on the state of nutrition. In rickets attended with marked dystrophy the influence of the latter is manifested to a greater extent. For example, in children with second and third degree hypotrophy the phosphorus in the blood in all forms of rickets is 2-3.1 mg% and that of calcium—6-7.9 mg%.

The functional state of the gastrointestinal tract in large

measure determines, in addition to other factors, the change in mineral metabolism. In children with an unstable stool hypophosphatemia and hypocalcemia are more strongly pronounced. Particularly significant are the changes in calcium metabolism. In children with second and third degree rickets and normal motor intestinal function the blood calcium is 9-8.7 mg% and in those with an unstable stool—8-7 mg%. This is easy to understand if we recall that in the healthy organism the splitting, absorption and intermediate metabolism of organic and inorganic mineral compounds are connected with acidity of the gastric juice, which determines the reaction of the medium in the upper portions of the intestinal tract, with the function of the liver, the normal activity of the enzymes and hormones, vitamin sufficiency, the motor function of the intestines and many other factors. In rickets, especially if it is combined with nutritional disorders, the functions of the gastrointestinal tract are disturbed. The acidity of gastrointestinal juice diminishes, the enzymatic activity weakens and the function of the liver and pancreas is altered; these factors intensify the changes in water, protein, fat, carbohydrate and mineral metabolism.

Disturbance of the bile-forming function of the liver leads to a diminution of the bile in the intestinal lumen, which circumstance affects the processes of assimilation and metabolism of mineral substances. The dyskinetic intestinal disorders attendant upon rickets considerably increase the mineral deficiency and are thus conducive to intensified excretion of calcium and phosphorus from the organism.

Seasonal variations in blood phosphorus and calcium can be noted in rickets. I. V. Tsimbler and L. L. Begam found the phosphorus in the blood of children with clear clinical symptoms of rickets 2.7 mg% in March, to increase to 5 mg% from April to June and to decrease to 4.5-4.2 mg% in July-November, and to 3.9 mg% in December.

According to the author's findings, the lowest phosphorus level (an average of 2.9 mg%) was in January; it rose

in February and March and reached its highest in April (3.8 mg%); it persisted on that level until October and began to drop in November. The highest calcium level was noted in October-November (an average of 10 mg%); in January it was 8.6 mg%, in February—8.2 mg% and in March—7.2 mg%. Such a considerable drop in the calcium level of the blood in March-February is apparently connected with increased insolation, under the influence of which the processes of vitamin D formation in the child's organism improve, leading to improvement in phosphorus metabolism and greater deposition of phosphorus and calcium salts in the bones, thereby decreasing the calcium in the blood.

The studies of I. A. Shabad et al have helped to elucidate the reason for the diminution of mineral substances in the bones during rickets, but the conditions leading to insufficient impregnation of the growing cartilage and newly-formed bone with mineral salts and to intensified excretion of phosphorus and calcium from the organism are still unclear.

Later investigations of Soviet and foreign authors were aimed at elucidating the biochemical changes in the patient's blood and tissues, and at determining the physical conditions of solubility of phosphorus and calcium compounds and the chemical composition of the bone substance. The discovery of vitamin D (1922) made it possible to offer more definite suggestions about the pathogenesis of rickets.

According to the conclusion drawn by György and Freudenberg, a deficiency of vitamin D in the child's organism provokes metabolic disorders. Phosphorus metabolism is the first to be altered. A diminished splitting-off of inorganic phosphorus from its organic compounds results in hypophosphatemia. Phosphorus (ionised) actively participates in carbohydrate, fat and protein metabolism, forming a series of organic compounds with the intermediate products of metabolism of these most important substances

which are links in the endless chain of their transformations in the organism. In hypophosphatemia metabolism slows down and the oxidative processes diminish. Large amounts of unoxidised products of intermediate metabolism accumulate in the blood and acidosis develops. In an attempt to normalise the acid-base balance the organism excretes mainly with the urine a large amount of phosphates, owing to which hypophosphatemia increases still more. Both hypophosphatemia and acidosis are conducive to disturbances in the process of ossification. Deposition of calcium in the newly-formed tissue occurs at a pH of 7.3-7.35 (Kramer), a more acid medium inhibits the deposition of calcium salts, while at a pH of 7.1 this process almost completely ceases. As a result, the osteoid tissue is insufficiently impregnated with salts and osteogenesis is disturbed.

Contrary to the foregoing view Howland and Kramer (1925-27) held that hypophosphatemia in rickets was a result of a disturbance of phosphate absorption in the intestines, owing to which the tissues were deficient in PO_4. However, this theory is at variance with the hyperphosphaturia observed in rickets. Moreover, subsequent observations have shown that the absorption of phosphates in the intestines is not disturbed. Enteral administration of phosphorus to rachitic children appears to increase its content in the blood serum with its subsequent diminution within 4 hours (G. A. Khain, 1928). In an experiment with radioactive phosphorus it was established that vitamin D does not specifically affect phosphorus adsorption in the intestines of rachitic rats (B. A. Kudryashov).

Some authors have suggested that hypophosphatemia appears in rickets as a result of diminished phosphorus ethers in the blood and, consequently, decreased phosphorus compounds required for the process of ossification (Bodansky, Kay).

The results of research and the suggested theories indicated a definite influence of vitamin D on mineral me-

tabolism and a connection between its deficiency and the altered phosphorus-calcium index in rickets. However, the mechanism of action of this deficiency in the development of hypophosphatemia remained unclear.

Many authors hold that the transition of phosphorus and calcium compounds from the blood to the organic bone substance is directly dependent on the presence of vitamin D in the blood. Causeret established (1953) that the presence of even small amounts of vitamin D in the food was conducive to increased calcium in the organism.

Studies of mineral metabolism in rachitic and normal animals by administration of radioactive isotopes of phosphorus and calcium have shown that during the first hours the bony tissue of rachitic animals absorbs them more intensely, but does not retain them long (Y. A. Perkovich, 1956). Claassen and Wöstmann found (1957) that 24 hours after intravenous administration of P^{32} much less (50 per cent) calcium salts was fixed in the bones of rachitic animals than in those of normal animals.

These experimental studies were confirmed by Bauer, Carlsson and Lindquist (1956) who discovered a much lesser deposition of phosphorus and calcium salts in the bones of children with incipient forms of rickets when introduced into the organism from without than in healthy children of the same age. Administration of vitamin D normalised the process of calcification.

The action of vitamin D is, consequently, directed towards establishing a definite correlation between the content of phosphorus in the blood and the tissues, as well as between inorganic phosphorus and calcium in the blood, corresponding to the normal process of deposition of phosphorus and calcium salts in the bones.

The foregoing concepts of the pathogenesis of rickets explain mainly the disturbances in the bones, but the other pathological phenomena which characterise the clinical picture of the disease are still unclear. The shortcoming of the suggested theories is that they view all the changes

discovered in the rachitic process from a purely chemical standpoint, in isolation from the other metabolic processes in the organism. These theories overlook, in the development of the pathophysiological symptoms, the integrity of the organism, the interrelations of all the biological processes operating in it and the regulating influence of the central nervous system on all metabolic processes and regulatory mechanisms.

It is impossible to form a correct idea of the pathogenesis of rickets without taking the role of the nervous system into account. The first manifestations of rickets are symptoms attesting a disturbance in the central and vegetative nervous systems. Increased excitability of the child, excessive sweating, sleep disturbances, loss of appetite, gastrointestinal dysfunction and muscular hypotonia are all signs of it. N. I. Krasnogorsky has demonstrated that the incorrect and perverted metabolism in rickets causes a disturbance in the functions of the cerebral hemispheres and diminishes the excitability of the cortical cells. This results in deep changes not only in the acquired cortical reactions, but also in the inborn extracortical reflexes which constitute the basic stock of activity and underlie the whole of the complex system of cortical regulations.

Experimental studies (N. O. Skolskaya, 1956) have established marked morphological changes in the cerebral tissues of rachitic animals. These include tumescence and edema of the pia mater, hyperemia of the cerebral substance and distention of the ventricles. In addition to hyperemia of the pia and the brain substance, and their increased permeability, with phenomena of diapedesis, histological examination has also revealed inflammatory changes in some parts of the cortex and the subcortical layer. At the same time dystrophic changes in the neural elements (swelling and vacuolation of the cytoplasm, dissolution of the basophilic substance and tumefaction of the nuclei) are found in the cerebral cortex, the white matter and the subcortical ganglia. It may be assumed that

rachitic children have similar morphological changes in the cerebral tissues and that these changes underlie the functional disturbances in the nervous system.

Y. M. Lepsky and G. A. Reshetnikova (1953) demonstrated experimentally that the nervous system plays an important part in the pathogenesis of rickets. For example, in animals kept on a rachitogenic diet but simultaneously administered proserine (neostigmine) rickets did not develop, as it did not in rats given vitamin D. Animals who, in addition to a rachitogenic diet, were administered ephedrine exhibited rickets, as did all the other rats kept on a rachitogenic diet. Thus, the drug acting on the cholinergic structures, by stimulating the parasympathetic division of the nervous system, prevented development of experimental rickets, while the substance acting on the adrenergic structures failed to prevent it. It follows that stimulation of the sympathetic division of the nervous system does not prevent rickets.

These experimental data were confirmed by observations in the clinic (I.B. Baskina). Inclusion of proserine in the complex of therapeutic measures produces a favourable effect in that it improves the psychomotor functions and hastens normalisation of the metabolic processes.

An important part in the development of rickets is played by the state of the endocrine glands. P. S. Medovikov was the first to suggest that the hormonal-vegetative changes observed in this disease cause a disturbance in the ion equilibrium and thereby affect the nervous system, which is subsequently responsible for the disturbance in the metabolism of mineral substances. The first to suspect hyperfunction of the parathyroids in spontaneous rickets was Erdheim (1914) who discovered them to be enlarged in experimental animals. Somewhat later Ritter found a similar enlargement in rachitic children. This new fact aroused still greater interest after Collip's studies (1925) in which a special substance raising the calcium level in the blood was isolated from the parathyroids. How-

ever, the pathogenic connections between these factors were not as yet established.

Observations conducted by G. A. Khain in 1935 showed that in experimental rickets in rats kept on a calcium-rich diet the parathyroids considerably contracted, whereas in rats given food containing little calcium the development of rickets involved enlargement of the parathyroids. Experiments have demonstrated that the enlargement or contraction of the parathyroids depends on the amount of calcium contained in the animals' food. Calcium deficiency in the diet causes a compensatory increase in the hormonal function of the parathyroids, mobilising the calcium from the bony tissue. When vitamin D is administered to rachitic animals, the parathyroids contract, and do so the faster, the higher the daily dose of vitamin D (P. M. Mamish, 1953). The results of these experiments have shown that there is a connection between the hormonal function of the parathyroids, vitamin D and the amount of calcium in the food.

It was subsequently established that the regulation of calcium metabolism involves, in addition to vitamin D and the parathyroids, also the thyroid, the anterior lobe of the hypophysis and other endocrine glands. For example, Arvy and Gabe discovered hypofunction of the thyroid in experimental rickets (1950). Administration of thyroxin, like that of vitamin D, lessened the disturbance in carbohydrate metabolism, the phenomena of anemia and other pathological symptoms.

Disturbance of the hormonal function of the adrenals plays a definite part in the pathogenesis of rickets. Hanssler (1956) demonstrated the favourable effect of cortisone on the process of calcification in the metaphyses, when administered to rats kept on a rachitogenic diet.

It had long been believed that the parathyroid hormone acted primarily on calcium metabolism, while the changes in the phosphorus metabolism were a secondary phenomenon. However, the studies that were soon published con-

vincingly demonstrated the fallacy of this view. It was experimentally discovered that in pups kept on a rachitogenic diet the tubular reabsorption of phosphates diminished and that it sharply increased upon administration of vitamin D.

Injection of parathyrin further decreases the reabsorption of phosphates from the renal tubules into the blood, which leads to hypophosphatemia (Harrison, 1941).

Considerable disturbances in the process of reabsorption of phosphorus in the kidneys of rachitic children were discovered by K. A. Svyatkina (1952-54). According to this author, the reabsorption of phosphates in the renal tubules of healthy children averaged 83.5 per cent with respect to filtration, while the blood contained about 4.5 mg% of inorganic phosphorus. In the incipient stage of rickets reabsorption equals 43 per cent, at the height of the second and third degrees of the disease it is respectively 36 and 33.8 per cent (the blood contains about 2.8 mg% of inorganic phosphorus) and during convalescence—51.4 per cent.

Administration of vitamin D improves tubular reabsorption of phosphates, and within 3-4 weeks (in severe forms somewhat later) increased phosphorus in the blood is observed (K. A. Svyatkina, Freeman and Dunsky).

In rickets tubular reabsorption of amino acids also diminishes. In healthy children 98 per cent of the amino acids is reabsorbed in the tubules, in rachitics—only 90 per cent (Berger, Stalder, 1956). Aminoaciduria disappears within one or two months of treatment with vitamin D_2 or D_3 (P. Royer, 1956). This fact suggests the idea that diminished tubular reabsorption of amino acids is connected with vitamin D deficiency. Considerable excretion of amino acids in children with active rickets disturbs the protein metabolism and alters still more the balance of mineral substances, since assimilation of phosphorus and, especially, calcium is closely connected with the presence of enough proteic substances in the organism.

Thus it has been ascertained that in rickets hypophosphatemia, which consistently causes further disturbances in metabolism (primarily calcium metabolism), develops as a result of the changes in the process of reabsorption of phosphates in the renal tubules due to intensified formation of parathyrin. By stimulating the process of reabsorption of phosphates and amino acids in the kidneys and producing an increase in blood phosphorus and calcium, vitamin D plays an important part in the mechanism of balancing phosphorus and calcium metabolism.

Disturbance of the acid-base balance in the direction of acidosis is conducive to development of hypophosphatemia. The alkaline reserve of the blood in rachitic children diminishes at the height of the disease to 33.2-38.6 per cent by volume of CO_2 (E. A. Reikher and co-authors, K. A. Svyatkina). While acidosis is not a direct cause of the disease, it plays a big part in the genesis of the subsequent pathological changes. It has been established that the acidotic state leads to parathyroid hyperfunction (A. V. Rusakov) and, consequently, to phosphorus and calcium deficiency in the organism. In acidosis the phosphorus and calcium compounds in the blood are in solution and are not deposited in the cartilaginous and osteoid tissues of the growing bones, owing to which the processes of osteogenesis are disturbed. Even this circumstance alone shows what harmful influence acidosis exerts on the organism of the rachitic child.

Thus, the interaction of the factors conducive to a disturbance in the normal correlation between the various ingredients in metabolism leads to rickets.

The role of phosphatase ("bone enzyme"), discovered in 1923 by Robison during his histochemical studies of the process of calcification, is not quite clear in the pathogenesis of rickets.

Phosphatase is found in large amounts in growing bone and ossifying cartilage and is not found in non-ossifying cartilage, for example, the trachea. That phosphatase par-

ticipates in the process of bone formation is proved by its appearance in embryonic tissue at the time osseous tissue is being formed.

In the blood phosphatase is found in small amounts which change at the different periods in the life of the organism. The enzyme appears to be most active during the first days of the child's life—up to 16 u (Bodansky) as against the 2-3 u in the mother.

The normal amount of phosphatase in infants is considered to be 0.17-0.34 u per 1 ml of blood serum by Kay's method and 4-5 u per 100 ml of blood serum by Bodansky's method.

An important role in the processes of ossification is assigned to phosphatase because of its splitting action on phosphoric ethers with liberation of acid required for the formation of phosphorus and calcium compounds. At a definite hydrogen ion concentration (pH 7.5-7.4) calcium salts are precipitated from the blood which bathes the osseous tissue and react with the available phosphorus to form $Ca_3(PO_4)_2$ which is deposited in the newly-formed bony tissue and cartilages. Phosphatase regulates the content of inorganic phosphorus at the sites of ossification. Acidosis in rickets interferes with the activity of phosphatase. Slight changes from pH 7.4 to 7.1 in the medium at the sites of ossification sharply inhibit the process of formation of calcium salts of phosphoric acid. Diminished activity of phosphatase may be one of the reasons for it, since its optimum action is possible at pH 7.5-7.8 and higher.

There is as yet no agreement on the question of the changes in the activity of phosphatase in rickets. Y. M. Lepsky, L. A. Yuryeva, M. B. Kokhanova, G. G. Shuneiko and K. A. Svyatkina hold that phosphatase becomes more active even before the appearance of clear clinical symptoms of rickets, its activity increasing with the intensification of the process and continuing for some time after disappearance of the symptoms of the disease.

Other authors do not note such sequence and dependence on the gravity and development of the disease. Y. F. Dombrovskaya, M. I. Dementyev, S. A. Novikov, Y. P. Kratinova, P. Y. Levitina and A. M. Kirkevich have found that the content of phosphatase in the blood does not always correspond to the severity and dynamics of rickets since it reflects the influence of many factors on the child's general condition and reactivity, for which reason determination of the activity of this enzyme is of no diagnostic value.

Giraud, Vincent and Coignet (1949) found the activity of phosphatase to be increased only in one-third the rachitic children they examined. In the others the amount of alkaline phosphatase was normal or diminished despite the clear clinical picture of a rachitic process confirmed roentgenoscopically.

In an experiment with white rats diminished activity of both serum alkaline and bone phosphatase was observed on the appearance in the animals of symptoms of rickets caused by an inadequate (phosphorus-deficient) diet (Dikshit and Chitre, 1950).

According to the author's data, activity of alkaline phosphatase increased from 6 to 15 u in 12 per cent of the rachitic children, while in 67 per cent the activity of the enzyme was between 4 and 6 u. In the rest of the children (21 per cent) the activity of the enzyme was diminished.

The author did not succeed in establishing any dependence of the increase in phosphatase activity on the severity of rachitic manifestations. In the mild form of rickets (first degree) the activity of the enzyme is in some cases more intense than in moderately severe and severe forms. The indices of phosphatase activity vary widely in different children affected with rickets of the same severity. In first degree rickets the amount of phosphatase in some children may be between 10 and 12 u, in others—between 4.3 and 4.5 u; in second degree rachitics phosphatase activity varies between 2.7-3 and 9-15 u.

The changes in phosphatase activity in rickets are directly dependent on the state of the child's nutrition. For example, in normally nourished children with first degree rickets the amount of phosphatase averages 8.3 u and in children affected with dystrophy—4.3 u; in normally nourished children with second degree rickets phosphatase activity is 7.6 u, whereas in second and third degree dystrophy it is 3.8 u. It follows that increased activity of alkaline phosphatase in the blood during rickets is more constant only in children of satisfactory nutrition; in rickets involving dystrophy the phosphatase is unaffected or, more frequently, diminished (D. K. Itskovich, G. G. Shuneiko, M. N. Bessonova).

After vitamin D and ascorbic acid therapy of children with very active phosphatase the activity of the latter diminishes, while in children with a low phosphatase level the latter is observed to rise over a period of 3-4 months, when the children are clinically already recovering from rickets. By the end of the fourth or fifth month the phosphatase level of all children administered vitamins D and C returns to normal, i.e., 4.6-5.7 u.

Some studies have confirmed the stimulating effect of vitamins D_2 and D_3 on the activity not only of blood alkaline phosphatase, but also on that of renal, intestinal and bone phosphatases. It has been demonstrated experimentally that in animals kept on a rachitogenic diet the activity of alkaline phosphatases diminishes, while addition of phosphorated vitamin D (D_2P) or D_3 to the food causes the activity of phosphatases to increase (Zetterström, Ljunggren and Löhr, 1951).

Diminished activity of the serum alkaline phosphatase in animals resulting from vitamin C deficiency has been established experimentally (S. I. Vinokurov and Z. I. Spilioti) and has been verified in the clinic by L. L. Gural and Y. M. Mironova. According to these authors, lower phosphatase activity corresponds to lesser vitamin C content in the blood plasma. Administration of ascorbic acid to

patients, while reducing the biochemical indices of vitamin C deficiency, stimulates increased activity of the serum alkaline phosphatase; with normal vitamin C content in the blood (0.9-1mg%) the activity of phosphatase is 4-6 u, i.e., normal for healthy people.

In rickets the author established the same correspondence between the content of ascorbic acid and the activity of the enzyme. In this case the more marked vitamin C deficiency, the lower the level of alkaline phosphatase in the blood. From 0.1 to 0.29 mg% of ascorbic acid corresponds to an average of 3.2 u of phosphatase activity; with 0.3-0.49 mg% of vitamin C in the blood the phosphatase level is 4.8 u; in a state of saturation (0.9-1.2 mg%) of the organism the activity of the enzyme increases to 7-8 u. It follows that vitamin C deficiency observed in rickets often runs parallel to diminished or weakened activity of the alkaline phosphatase of the blood.

Inclusion of ascorbic acid in the complex of therapeutic measures leads to an increase in the content of the enzyme. Our inferences that vitamin C greatly activates many of the blood enzymes, including phosphatase, are confirmed by the findings of B. A. Kudryashov, B. I. Zbarsky, Badinand, Meyer and Voegtein.

A correspondence between the activity of phosphatase and the level of inorganic phosphorus in the blood is also observed. In the overwhelming majority of cases with 3 mg% phosphorus and 8.4 mg% calcium the activity of phosphatase is 4 u, whereas normal phosphorus and calcium content corresponds to 6-6.6 u of phosphatase activity.

The studies conducted by the author, like those carried out in the Pediatric Clinic of the First Moscow Medical Institute, have shown that in most rachitic children the vitamin C content in the blood is considerably diminished.

A marked vitamin C deficiency was discovered in 39 per cent of the children, a perceptible decrease in vitamin

C—in 52 per cent and a satisfactory saturation index was found only in 9 per cent of the cases.

The ascorbic acid deficiency is greater in children with severe forms of rickets: the amount of vitamin C was 0.1-0.29 mg% in 39.7 per cent of the children with second degree rickets and in all children with the severer form (third degree) rickets. In cases of equal gravity the lowest saturation is observed at the height of the disease. But even in the initial stage of first degree rickets in infants (up to 1 year of age) biochemical indices (0.1-0.2 mg%) attesting considerable ascorbic acid deficiency are found in the overwhelming majority of cases. This signifies that the organism of the child becoming affected with rickets is already considerably deficient in vitamin C and the clinical picture of the disease develops against the background of vitamins D, C and, as will be shown below, B_1 deficiency.

The disturbance in vitamin C metabolism in rickets is also due to a number of other causes. The state of the child's nutrition has been found to play an important part. In severe forms of rickets considerable deficiency (0.1-0.2 mg%) is found in 23.4 per cent of the normally nourished children, in 33.7 per cent of children with second degree hypotrophy and in 62.5 per cent of the children with third degree hypotrophy.

The ascorbic acid content in the blood of children during the first year of life with the same severity and stage of the disease, as well as the same state of nutrition, is much lower than in older children. This is conditioned primarily by the character of feeding. In winter and spring the child does not recieve enough vitamin C with the mother's milk. Human milk drawn off between January and May contains about 1.3-1.5 mg% ascorbic acid; in June-August the content increases to 2.15-2.8 mg% and in October to 3.3-3.5 mg%; in November it begins to decrease again (M. N. Bessonova). In boiled donor's milk ascorbic acid is 0.4-0.6 mg% lower than it is before boiling. The

usual milk mixtures for feeding infants contain only one-ninth or one-tenth the ascorbic acid found in human milk (N. P. Shastin).

The balance of vitamin C in the organism is closely connected with that of the other vitamins, including vitamin D. After treatment with vitamin D_2 its balance improves. Within one month of the treatment the amount of vitamin C in the children's blood doubles—from 0.2-0.3 to 0.57-0.68 mg%—without its additional administration and with the same food ration as before the treatment. Subsequently the amount of vitamin C increases very slowly and only within 2-3 months reaches normal indices, i.e., 0.9-1 mg%.

In rickets the balance of riboflavin and thiamine is also observed to decrease.

According to literature (M. A. Straukh and G. A. Malchenko), the normal content of vitamin B_1 in the blood of healthy infants averages 4-5 γ %. Considerable thiamine deficiency has been found in all children affected even with mild forms of rickets. From traces to 1.2-1.4 γ % of it was found in 60 per cent of the examined children, from 1.5 to 2 γ %—in 28 per cent of the children, and between 2.2 and 3.5 γ %—in the rest of the children (M. N. Bessonova and A. F. Nesterina).

Vitamin B_1 deficiency depends more on the period of the disease than on its form. Thus, at the height of first degree rickets the content of vitamin B_1 averages 0.5-0.6 γ % (in individual children—from traces to 1 γ %), in second degree rickets—0.3-0.4 γ % (from traces to 0.8 γ %); during convalescence its amount increases 3-5-fold and averages 1.5-1.8 γ % (with variations between 0.8 and 3.3 γ %).

The greatest deficiency is observed in infants during the first year of life, especially, in cases of nutritional disorders. In first degree rickets the amount of vitamin B_1 in hypotrophic children decreases from 0.8-0.5 γ % to traces, while in normally nourished children, all other

things being equal, its content in the blood is 0.5-1 γ % higher.

It follows that in all forms of rickets the overwhelming majority of children have marked vitamin B_1 deficiency; moreover, the greatest deficiency is at the height of the disease in nurslings and in cases of chronic nutritional disorders. Taking into account the great importance of vitamin B_1 in metabolic processes, it must be recognised that vitamin B_1 deficiency is one of the factors which aggravate the course of rickets, especially since the deficiency of this vitamin is conducive to development of dystrophy (E. I. Fridman, I. V. Tsimbler, H. L. Emdina, V. A. Leonov and Y. F. Dombrovskaya).

Saturation with ascorbic acid perceptibly reduces thiamine deficiency. With an increase in vitamin C content in the blood to 0.8-0.9 mg% the content of vitamin B_1 reaches 3-4 γ %, which confirms the interdependence between these vitamins in the metabolic processes of the organism.

The influence of vitamins B_1 and C on mineral metabolism is indubitable. Vitamin B_1 participates in fat metabolism and in processes of phosphorylation, i.e., in processes closely connected with phosphorus and, consequently, calcium metabolism. The role of this vitamin is important also because it is a regulator of the secretory, motor and absorbing functions of the gastrointestinal tract. Vitamin B_1 deficiency leads to accumulation of pyroracemic and lactic acids in the organism, i.e., products of intermediate carbohydrate metabolism, which aggravates acidosis.

Aggravating the disturbances of the oxidative, reductive and other metabolic processes in rickets vitamin C and B_1 deficiency may lead to weakening of the regulatory functions of the central nervous system and thus greatly influence the development and subsequent course of the rachitic process.

By aggravating the disturbances in metabolism the deficiencies in vitamins B and C observed in rickets are conducive to development of graver forms of the disease.

CLINICAL ASPECTS

The first to be observed in the clinical picture of rickets in infants in the very beginning of the disease are dysfunctions of the nervous system. The infants become irritable, frequently cry without apparent cause, are frightened by the slightest sounds and sleep very poorly. They develop increased vasomotor excitability, slight pressure on the skin leaving red spots. Dysfunction of the gastrointestinal tract is observed. Excessive sweating is one of the early manifestations of rickets. Even with a moderate temperature in the room and not overly warm clothes the child's body is usually moist. A fine eruption elevated above the surface (prickly heat) can be observed on the skin of the neck and body and in the skin folds. The excessive sweating of the infant is manifested particularly clearly during nursing and sleep, the infant's head sweating so much that the pillow not infrequently becomes wet. The sourish, sticky sweat irritates the skin and makes the child uneasy so that the child keeps turning the head from side to side. Because of the continuous rubbing of the head against the pillow the hair begins to fall out and the child develops a bald patch on the occiput; the venous network on the head becomes visible.

All the aforesaid is connected with complex processes operating in the central and peripheral nervous systems. In rickets the intracranial pressure is elevated and the protein in the cerebrospinal fluid is diminished, which de-

notes peculiar hydrocephaly. The disturbance in mineral metabolism, especially the deficiency of the organism in phosphorus, unfavourably affects the metabolism in cerebral tissue. Developing acidosis also impairs this metabolism. Alterations in the functions of the digestive organs and the frequent, unstable stool are conducive to development of hypovitaminoses to which the nervous tissue is very sensitive. In addition to the biochemical changes, rickets apparently also involves morphological changes in the nervous system which determine the functional disturbances observed already during the incipient stage of the disease. As was already mentioned in the chapter on the pathogenesis of rickets, some experimental data seem to indicate this.

The reactivity of the vegetative nervous system in rachitic children is subject to considerable individual variations and remains modified not only in the initial period and at the height of the disease, but in a considerable number of children also during convalescence.

Y. I. Muratidi discovered a peculiarity in the thermoregulating mechanisms manifested in a big difference (from 0.1 to 3.1°C) in the temperature of the skin at symmetrical sections, compared with healthy children in whom this index averages 0.2°C, in an altered thermoregulation reaction (to heat stimulation) which is either prolonged or perverted, and in a difference in the intensities of perspiration at symmetrical points of the forehead and palms of the hands. During convalescence these thermoregulation reactions return to normal.

The vascular reaction of the skin determined by the method of dermographism is unequally manifested during different periods of the disease. During the initial period of first degree rickets stable red dermographism is observed almost in all children.

At the height of second and third degree rickets this reaction is clearly pronounced only in 40-50 per cent of the children and diminished in the rest. In children with

rickets complicated by dystrophy red dermographism is barely observed or is absent.

The clearest clinical symptoms of rickets are changes in the *osseous system*. The changes in the bones occur at different times and unevenly through the skeleton. The earliest and most intense disturbances take place in the rapidly growing bones—the skull, anterior ends of the ribs, and metaphyses of the tubular bones; changes in the vertebrae, pelvic bones and jaws occur later. That is why the bone symptoms in rickets vary with the patient's age: infants during the first six months of life exhibit affections of the skull and thorax, older children—of the limbs and spine.

The first sign of affection of the osseous system during the incipient period of rickets is a softening and pliancy of the parietal and occipital, less frequently the temporal and frontal, bones, and of the margins of the anterior and posterior fontanels. Similar softened sections are observed along the cranial sutures. Craniotabes usually occurs in infants during the first months of life. Observing 712 infants from the moment of birth Z. G. Korolyova discovered craniotabes in 84 of them (11.8 per cent) already between 5 and 12 weeks of age. In these infants the diagnosis of rickets was confirmed roentgenoscopically and biochemically. The squama occipitalis is the earliest to soften, especially in prematurely born children. On palpation the occipital bone feels like parchment.

The head of a rachitic child is disproportionally large because of the greater development of the cerebral part of the skull and the retarded growth of the facial bones and the base of the skull (Fig. 1).

Owing to the softness of the bones the skull may assume irregular shape (sloping, flattened, etc.) in accordance with the child's position in bed. Subsequently severe forms of rickets may cause deformities—frequently very stable—of the jaws. The upper jaw may become elongated anteroposteriorly and protrude in front over the lower

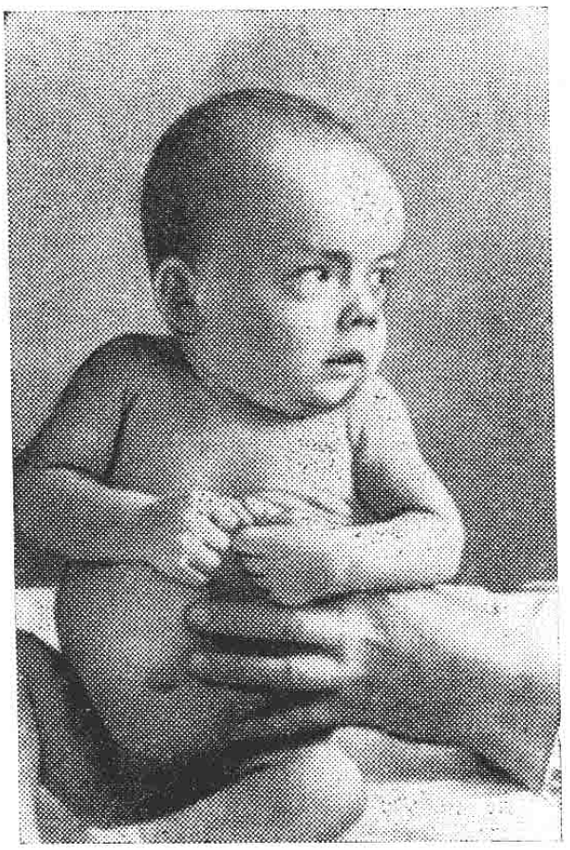

Fig. 1. Head of rachitic child

jaw, while the lower jaw becomes angular and flattened in front. This disturbs articulation. The hard palate becomes high and narrow. A narrowing of the nasal passages may result. The anatomical and physiological prerequisites for the appearance of deformities are the coincidence of the period of intensive growth of the lower jaw with the height of the disease and the close dependence of the development of this bone on the state of the masticatory muscles and articular ligaments (L. V. Ilyina-Markosyan).

Bosselated frontal and parietal eminences may appear very early—in the second or third months (S. O. Dulitsky, L. B. Leivikov).

Various stable deformities of the skull are observed in accordance with the severity and course of the disease, the state of the child's nutrition and the intensity of treatment. Because of the excessive growth of the parietal and bosselated frontal eminences the skull may assume different shapes (square, clinocephalic, brachycephalic, olympian forehead). The anterior fontanel closes late (towards 16-24 months of age). Owing to the general changes in the shape of the skull the anterior fontanel also alters its shape from rhombic to square, triangular or stretched longitudinally and transversely; the sutures also close late (Y. F. Dombrovskaya).

In rachitic children the milk teeth often erupt in an irregular sequence and at later periods, although in some cases they erupt normally. In severe forms of rickets this

symptom is observed in the overwhelming majority of rachitics. According to the author's data, at the height of second degree rickets the teeth appear late in 58 per cent of the children and in third degree rickets—in 78.8 per cent. The teeth of rachitic children have defective tissues (dentin, enamel) and are easily affected by carious processes. Dental caries and fragility are due to vitamins C and D deficiency. Dental dystrophy is based on protracted mineral deficiency.

Rachitic changes in the bone-cartilage junctions of the ribs become evident simultaneously with craniotabes or somewhat later. At the junctions of the ribs with their cartilages nodules appear as a result of excessive growth of osteoid tissue; these nodules, so-called rachitic rosary, are particularly marked from the 5th rib down. The appearance of a rachitic rosary is usually observed in infants at the height of the disease. During the period of residual phenomena this symptom shows that the child had second or third degree rickets. It should be remembered that physiological thickenings at the bone and cartilage junctions of the ribs are sometimes observed in normal infants during the first months of life (Y. N. Yaroshevskaya).

The development of thoracic deformities in children affected with severe forms of rickets plays an important part in the subsequent respiratory and cardiovascular disorders.

As a result of the softness of the ribs and their greater mobility, a horizontal groove approximately corresponding to the attachment of the diaphragm (Harrison's groove) appears. This groove is particularly visible when the child cries or inhales deeply. During inhalation the false ribs part under the pressure of the abdominal organs, while the overlying true ribs are drawn in because of the elasticity of the lungs and the negative pressure in the pleural cavity. As a result the lower part

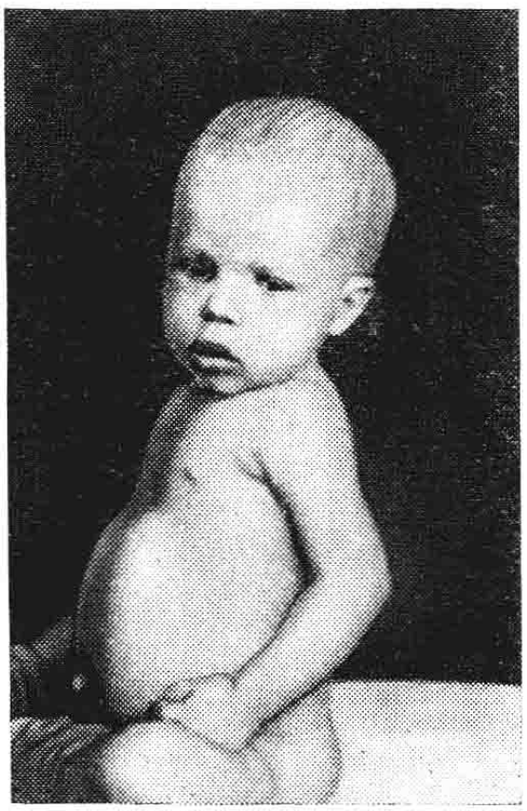

Fig. 2. Chest of a child with severe rickets showing Harrison's groove

of the thorax expands and the upper part contracts (Fig. 2).

In very severe cases, while the chest is greatly compressed from the sides, the sternum begins to protrude and so-called *pigeon breast* results. Sometimes the lower part of the chest is caved in (cobbler's chest).

Especially severe thoracic deformities are observed in curvatures of the spine (kyphosis, lordosis, scoliosis). They are a result of changes in the vertebrae, loosening of the ligamentous apparatus and lack of muscle tone.

The pelvic bones also undergo changes. Children who have survived grave forms of rickets may develop severe pelvic deformities due to retarded growth of the ilia and the changes occurring in the sacrum under pressure of the body weight. The pubic arch expands, the conjugate shortens, and a so-called flat rachitic pelvis results. Sometimes, under pressure of the heads of the femurs against the ilia, the lateral parts of the pelvis are also deformed. Such deformities are particularly important in girls because they may subsequently cause labour pathology.

Considerable changes in the bones of the upper and lower limbs are observed at the height of second and third degree rickets. Owing to the excessive growth of osteoid tissue so-called rachitic "bracelets" appear on the lower ends of the radius, ulna, tibia and fibula, and "pearl necklaces" on the phalanges of the fingers. Various forward and lateral curvatures of the thigh and forward

curvatures of the lower third of the shank occur. All these deformities are responsible for the formation of bowlegs (genu varum) and, knock-knees (genu valgum), flat feet (pes planus), etc.

Rachitic children usually lie on the back with their legs flexed and crossed. In these children the physiological curvature of the shanks increases because of the higher tone of the flexors and softening of the bones and leads to bowlegs; this condition is aggravated by the weight of the body if the child begins to stand or walk. But in cases of marked muscular hypotonia, which is observed in children with extreme nutritional disorders, no curvatures are noted even in severe forms of rickets with considerable softening of the bones. In cases in which the bones of the lower limbs soften later, after the children have begun to stand or walk, knock-knees develop as a result of the increased work of the extensors (S. O. Dulitsky).

In addition to the characteristic bone deformities and curvatures, the processes of disturbed bone formation and bone softening not infrequently lead to infractions and fractures.

The rachitic process hampers the growth of the bones in length. It is one of the causes of the arrested growth of rachitic children observed as early as the fifth or sixth month of life (Y. F. Dombrovskaya). The arrested general growth—a peculiar dwarfism—is particularly manifest in cases of changes in the vertebrae accompanied by deformities in other parts of the skeleton (Fig. 3).

Very severe forms of rickets leading to marked deformities of the osseous system now occur rather infrequently. But all the typical bone symptoms are still observed in various combinations, depending on a number of factors, in all forms of the disease.

Careful observation of children with rachitic manifestations reveals hyperplastic changes in the cranial bones (bosselated frontal and parietal eminences), a rosary, a thickening of the epiphyses of the forearm bones—"brace-

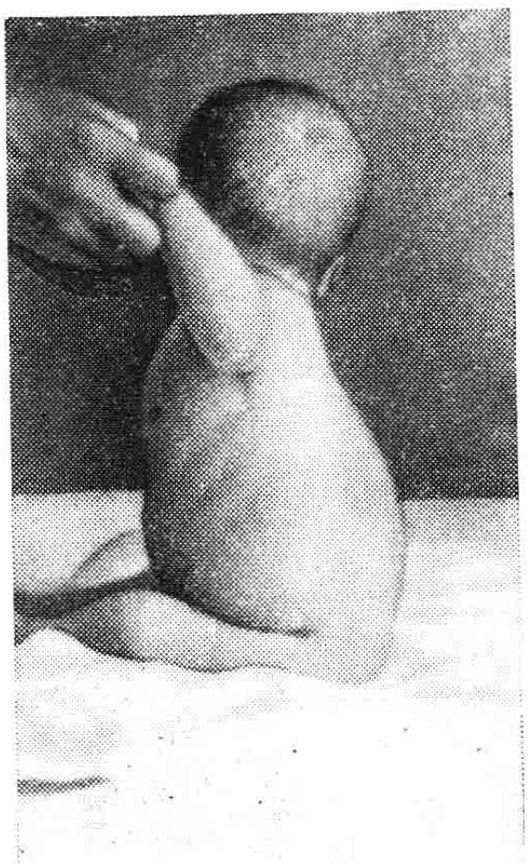

Fig. 3. Spinal curvature in a rachitic child. The head exhibits alopecia occipitalis

lets"; dystrophic changes—softening of the parietal and occipital bones and of the edges of the anterior fontanel, the increased size of the latter, pliancy of the ribs, which leads to various thoracic deformities, and other symptoms of the same character; phenomena of hypogenesis of osseous tissue manifested in late and irregular dentition, late closure of the anterior fontanel, retarded growth, etc. The foregoing symptoms are found in some measure in all forms of the rachitic process, but they vary in frequency and intensity with the form and period of the disease and the state of the child's nutrition.

Softening of the occipital bone and pliancy along the lambdoid and sagittal sutures and the edges of the anterior fontanel are observed in first degree rickets. A rosary and bosselated frontal and parietal eminences are a constant symptom.

Second degree rickets is characterised by much greater changes in the osseous system. Softening of the occipital and other cranial bones occurs rarely (only in cases of severe dystrophy), but pliancy of the edges of the anterior fontanel is observed much more frequently (in 40 per cent of the cases). The bosselated frontal and parietal eminences are not only a constant symptom (97.3 per cent—M. N. Bessonova); in addition, they also grow excessively in some children (16.9 per cent) and produce cranial deformities, namely, square skull and olympian

forehead (abnormally high and vaulted forehead). Deformities of the thorax (transverse constriction and eversion of the lower borders) are observed in 80 per cent of the cases, and curvatures of the lower limbs—in 33 per cent. The process of excessive growth of osteoid tissue in second degree rickets is also more clearly pronounced. For example, a rosary is found in 98.5 per cent of the cases (I. L. Abezgauz and S. A. Kushner), and a thickening of the epiphyses—in 35-40 per cent of all cases.

In this form of rickets irregular (34 per cent) and late (58 per cent) dentition and late closure of the anterior fontanel (15.8 per cent) can be observed.

The frequency and intensity of all the bone symptoms increase still more in children affected with third degree rickets. Thoracic deformities (pigeon breast) and rachitic kyphosis are not infrequently noted. Rachitic kyphosis is now observed less frequently—in 19 per cent of the cases in second degree and in 48 per cent of the cases in third degree rickets. L. L. Begam and S. A. Kushner (1937) cited much higher figures, namely: 20.6 per cent in first degree, 81.4 per cent in second degree and 92 per cent in third degree rickets.

The severity of the rachitic process is combined with deeper nutritional disorders. The deeper the nutritional disorder, the graver the skeletal deformity. This is connected with a deep disturbance in the process of bone calcification and osteogenesis, as well as with sharp muscular hypotonia in children with rickets complicated by dystrophy.

In addition to the afore-mentioned clear skeletal changes, mention must also be made of the pain symptom complex not infrequently observed in small children and manifested in crying out when attempts are made to put them on their feet or change their position.

It was believed that in rickets the bones were painful because the articular regions were filled with blood (A. B. Marfan). However, later studies have shown that in

a number of cases there is pain in the regions of the diaphyses and along the course of the nerves. In the former case it is a result of subperiosteal hemorrhages due to vitamin C deficiency, and in the latter—to vitamin B deficiency. The vitamin C deficiency in children with this pain symptom was confirmed by the author by biochemical blood tests. The author found the blood of only 25.8 per cent of the children to contain 0.4-0.44 mg% ascorbic acid, while that of the rest of the children contained 0.1-0.3 mg%. Vitamin B_1 deficiency was strongly pronounced in all the children (from 0.1 to 2 γ%).

Hyperesthesia observed in rachitic children can also be accounted for by trophic disorders. Of certain interest in this respect is the study of A. B. Lotin who conducted histological examinations of the bones of rachitic children. He discovered disintegration of myelin of nerve fibres and cellular infiltration in the connective tissue surrounding the neurovascular bundles which nourish the bones. According to this author, these phenomena may affect the nutrition and development of bone and be responsible for the pains occurring in the bones and muscles in rickets.

Muscular hypotonia is the most constant concomitant of rickets. According to Y. D. Zabludovskaya, various degrees of rachitic myopathy are observed in 97.8 per cent of rachitic children. The author's observations fully agree with these data. It is only because of the imperfect methods of examination that muscle lesions have not been found in all rachitic children. In rickets the muscles are thin and inelastic, their tone is low and contractions sluggish.

Considerable changes in the structural elements of striated muscle tissue have been established by experimental studies. These changes are manifested in diminished muscle fibres, deformation of their nuclei, disappearance of their cross striation, thickening of the endomysium and dilatation of the lumens of the endomysial blood ves-

sels. Considerable disturbances in the structure of the nerve fibres of the muscle tissue have been found, namely, thinning, intermittence and, in some places, granular disintegration of axial cylinders and deformation of their terminal branchings (A. A. Nikiforova).

Muscular hypotonia is connected with an altered content of phosphorus in the organism of the rachitic child. It is generally known that normal functioning of the muscular system is dependent on normal metabolism of phosphorus compounds which easily break up with liberation of phosphoric acid, and become synthesised again with absorption of this acid. In muscle tissue the phosphorus compounds are found mainly in the form of organic compounds. During physical work the organic phosphorus compounds rapidly break up in the muscles and part of the split-off phosphoric acid passes into the blood where the amount of inorganic phosphoric acid salts increases as a result. During rest organic phosphorus compounds are formed again and the inorganic phosphorus compounds pass from the blood into the muscles.

Creatinephosphoric acid is one of the substances that take part in the biochemical reactions connected with the functioning of the muscular system. During muscular contraction this acid breaks up into phosphoric acid and creatine which in its subsequent transformations is dehydrated into creatinine and is excreted in the urine. Diminished excretion of creatinine indicating diminished metabolic and functional processes in muscle tissue is observed in the rachitic process, especially if it is accompanied by marked myotonia (Y. P. Kratinova and P. Y. Levitina).

The severity of rachitic myopathy in children, especially in cases complicated by marked nutritional disorders, can also be accounted for by vitamin C and vitamin B group deficiency. Pathological phenomena in the nervous system responsible for the lowered muscle tone are found in cases of ascorbic acid and vitamin B_1 deficiency. Disorders of protein and carbohydrate metabolism

in cases of vitamin C and vitamin B group deficiency already during the initial stage of the development of the morbid process may cause considerable structural and functional changes in the muscular system of the rachitic child.

Studying the chronaxie in rachitic children R. B. Krasnova found it to be shortened in all the muscles she tested. According to this author, one of the causes of altered chronaxie at the height of the disease is a disturbance in the acid-base balance.

The deep changes in the structure of the muscle fibres and the greatly diminished electroexcitability (galvanic and faradic) warrant the assumption that rachitic myopathy is based on neurodystrophic disorders connected with dysfunction of the nervous system.

The extent of myopathy varies with the gravity and period of the disease and the state of the child's nutrition. At the height of severe forms of rickets this symptom is observed in all children. In cases of dystrophy combined even with mild forms of rickets muscular hypotonia is more strongly pronounced and after treatment persists for a long time in a considerable number of children.

Muscular hypotonia weakens the ligamentous apparatus and leads to abnormal joint mobility. In this condition the range of both active and passive movements is wider; lying on the back the child can draw its foot to the face and even put it behind its head.

One of the manifestations of *retarded development of the child's static and dynamic functions* is a clear manifestation of functional disorders in rickets. The child begins to sit up, stand and walk later, and ceases to walk if the disease develops at an older age.

The development of the static and motor functions is particularly retarded in children succumbing to rickets in the first months of life. At 6 months of age many of them cannot hold up their heads, at 12 months they cannot sit up without outside support and walk poorly up to

1.5-2 years of age. To help them out of this condition requires a great deal of effort.

The retarded development of the child's motor skills is due not only to hypotonia of the muscular system and the ligamentous apparatus; it is also connected with complex processes operating in the central and peripheral nervous systems. The basic cause of the retarded development of the motorium in rachitic children is a disturbance of the motor analyser. The proprioceptive stimuli coming from the muscles, tendons and joint surfaces are late in evoking the corresponding cortical impulses which lead to coordinated movements (N. I. Krasnogorsky).

The sluggish reaction of children to their surroundings and their apathy to the external environment denote a disorder of the functions of the cerebral cortex.

The rachitic process causes considerable functional and morphological *disorders of the respiratory organs.* Children with severe forms of the disease have visible dyspnea, a shallow inhalation and a difficult short exhalation, sometimes stertorous. The respiratory rate is 40-50 per minute. Clinical examination quite frequently reveals changes in the lungs, often manifested in weakened, laboured respiration with dry rales. In some cases moist rales are auscultated in the lower lobes of the lungs, the axillary region, along the paravertebral line in the back and along the edges of the sternum. Percussion yields a bandbox sound, but reveals no shortenings. The author observed such changes in 65 per cent of the children with moderately severe and severe forms of rickets. In cases of marked nutritional disorders these phenomena are more clearly pronounced.

There are many reasons for such respiratory disorders which complicate the condition of the rachitic child. At the height of the disease the deformed thorax, instead of expanding during inhalation, caves in on the sides. Without firm support the diaphragm contracts less vigorously and, as a result, the lungs do not expand enough either hori-

zontally or vertically. An important part is also played by hypotonia of all respiratory muscles and of the muscular layer of the diaphragm, and the high position of the diaphragm caused by distension of the intestines, meteorism and enlargement of the liver. Inadequate excursions of the thorax and muscular hypotonia result in formation of sections of diminished pulmonary ventilation and circulatory disorders. All these causes are conducive to atelectatic changes which result from obstruction with phlegm of the finer bronchioles pathologically altered in rickets (Y. F. Dombrovskaya).

Dynamic roentgenoscopy of the lungs in severe forms of rickets reveals, in addition to atelectases localised mainly along the sternum, enlarged bronchial nodes, emphysema and even circumscribed areas of pneumothorax (K. A. Moskachova and A. T. Martynenko).

Deep morphological changes occur in the pulmonary and bronchial tissues. Experiments on young rats kept on a rachitogenic diet show alternation of sections containing relatively little air with sections of emphysema, thickened interalveolar septa with their infiltration by lymphocytes and segmented cells, and dilatation of blood vessels (A. M. Khvul).

Children affected with rickets accompanied by hypotrophy have extensive changes in the alveolar epithelium with metaplasia due to vitamin A deficiency. All the changes in the lungs cause an oxygen deficiency which the child cannot resolve by accelerated external respiration, for which reason the organism uses up more respiratory enzymes and vitamins C and B_1. The amount of carbonic anhydrase which is an index of the respiratory function of the blood increases to 1.4-1.6, whereas in healthy children it is about 1.0 (Y. F. Dombrovskaya and Y. M. Valter). The increased need for ascorbic acid and thiamine, and the disturbances in their assimilation when consumed from without lead to their marked deficiency. The vitamin C, B_1 and D deficiency causes an oxygen deficiency and ag-

gravates the disorders of all forms of metabolism in the tissues of the brain and vegetative centres, for which reason the disturbances in the central regulation of respiration are the main cause of the disorders of the respiratory function in rickets.

The specific rachitic changes in the thorax, muscular hypotonia, morphological disorders of the pulmonary and bronchial tissues, diminished oxidative processes, altered gas content of the blood, disordered vitamin balance and mineral, carbohydrate and protein metabolism, which cause disturbances in the regulation of the respiratory centre, facilitate attacks of pneumonia and are responsible for its grave course often with unfavourable results. Children with second and third degree rickets are more often affected with pneumonia at the height of the disease than during the incipient period or convalescence (A. I. Perevoshchikova, L. S. Myakisheva, A. P. Smorchkov). In such children pneumonia runs a severe and prolonged course with aggravations, relapses, marked respiratory disorders, cyanosis and not infrequently attacks of asphyxia. Tissue respiration is impaired, which is attested by the gas composition of the blood and respiratory enzymes (carbonic anhydrase, glutathione) and vitamin C and B_1 metabolism (Y. F. Dombrovskaya, L. D. Shteinberg, S. O. Dulitsky). The changes in the lungs and the temperature reactions often do not correspond to the grave condition of the child affected with pneumonia. In infants with active manifestations of rickets, against the background of dystrophy, pneumonia is a disease of the whole organism, especially its toxic and toxicoseptic forms. Deep changes in the nervous, cardiovascular and digestive systems, and anemia, determine the severity and outcome of pneumonia (M. N. Bessonova, G. M. Borodina). Marked thoracic deformities and recurring pneumonias may lead to bronchiectasis, chronic pneumonias and carnification of the lungs.

Rickets causes disorders of the *cardiovascular function.* Many authors hold that in rickets the heart may be enlarged. According to Y. M. Lepsky, the border of cardiac dullness may be extended as a result of its closer adjacency to the thoracic wall caused by the high position of the diaphragm. In severe forms of rickets the heart may for a number of reasons really become enlarged. The sluggish contractions of the diaphragm and insufficient expansion of the thorax (pliancy of the ribs and hypotonia of the respiratory muscles), as well as the slight negative pressure arising on inhalation, do not exert the requisite suctorial action on the heart and large blood vessels, and hemostasis in the lungs and veins of the systemic circulation results. This creates unfavourable conditions for the work of the heart, especially its right half. The pliancy of the walls of the right ventricle facilitates distension of the heart. The development of cardiac insufficiency is fostered by hemostasis in the liver and branches of the portal vein. The amount of circulating blood diminishes. The meteorism observed in rickets becomes aggravated by the hemostasis and leads to still greater limitation of the movements of the diaphragm. A transverse position of the heart is observed in cases in which the diaphragm is high (S. O. Dulitsky).

Phosphorus metabolism disorders in rickets lead to diminished energy and trophic processes in the organism, particularly in the heart muscle. In cases of acidosis the disorder of the cardiovascular function is the greater, the more marked the disturbance in the acid-base balance. Anemia that accompanies rickets aggravates the oxygen want of the heart muscle, which in its turn intensifies the functional insufficiency of the cardiovascular system. It follows that cardiovascular dysfunction is directly associated with changes in many other organs and systems of the organism. The state of the central nervous system also plays an important part. The cerebral cortex exerts its regulating influence by perception, through sensory nerv-

ous apparatus located in the walls of the blood vessels, of the stimuli produced by changes in the chemical composition of the blood (chemoreceptors), intensity of arterial pressure (pressoreceptors), etc. The interoceptors transmit the stimuli to the corresponding nerve centres connected with the overlying cortical structures, whence the impulses are conveyed to the heart muscle (K. M. Bykov and I. T. Kurtsin). In rickets, especially when it is accompanied by dystrophy, the state of the central nervous system may serve as the cause of circulatory disorders owing to the weakened influence of the cerebral cortex on the state and function of the cardiovascular system.

Clinically it is easy to establish cardiovascular insufficiency which is clearly manifested in severe forms of the disease. Dyspnea, a greyish pigmentation of the skin and cyanosis of the visible mucous membranes are the most frequent symptoms of cardiac insufficiency in rachitic children. Congestive phenomena and elevated arterial pressure taking place in cases of insufficiency of the right heart account for the dilatation of the veins in the skin of the head and tumescence of the cervical veins clearly observed during examination of the children.

Percussion reveals dilatation of the right heart by 1-2 cm. The cardiac impulse is diffuse. Auscultation shows dull heart sounds and a delicate systolic murmur or unclear first sound at the apex. Tachycardia is most frequently observed, the heart rate in two-thirds of the children being 20-30 beats per minute faster than their normal age rate. According to Y. V. Abramova, the arterial pressure is, more often than not, elevated, the upper level being 115-125, the lower—60-70 mm Hg. In the electrocardiograms of children with severe forms of rickets the author noted a diminution of the waves (except wave T), extension of the QRS complex and the P-Q interval, and an increase in the systolic index. All these changes denote affection of the conduction system of the heart and of its muscular tissue.

In cases of severe nutritional disorders in rachitic children dilatation of the right heart, dull sounds, bradycardia, lowered arterial pressure—upper level to 70-80 mm and lower level to 40-50 mm Hg—are observed (M. N. Bessonova). This can be accounted for by a tonogenic dilatation of the heart muscle. According to Y. F. Dombrovskaya, in children with nutritional disorders the main factor in functional disturbances of the cardiovascular system is pathology of the vascular tone which is a result of pathological neurohumoral correlations and disturbance of the regulatory processes in the organism.

The rachitic process produces considerable changes in the *digestive organs*. In many children the oral mucosa is dry, lustrous ("lacquered") and bright red. Sections of mucosa bare of epithelium can be seen on the tongue—geographic tongue. In cases of clearly marked forms of rickets and considerable hypotrophy the mucosa of the gums may be edematous and cyanotic. Children in the second or third year of life quite often have transverse fissures on the lips, sometimes deep and bleeding; in the corners of the mouth they have hyperemia, fissures or ulcers. All these changes are symptoms of vitamin A, C, B_1, B_2 and PP deficiency which accompanies rickets.

External examination reveals increased abdominal girth in most of the children (in 82.6 per cent in second degree rickets and in 95 per cent in third degree). In shape the abdomen is distended to the sides and frequently has eminences—two on the sides of the linea alba and one in the upper part. These protrusions are particularly noticeable when the child tries to change his position or cries. The enlargement of the abdomen is caused by distension of the intestines in length and width, meteorism, and hypotonia of the muscular layer of the abdominal wall. On palpation the abdominal wall is pliant, the hand sinks in easily and there is an impression of "doughiness" (Fig. 4).

Rachitic children are found to have an enlarged liver both in the mild and the more severe forms of the dis-

ease—60 per cent in first degree and 80-95 per cent in second and third degree rickets. In many cases the spleen is also enlarged. Many suggestions are made concerning the reasons for the enlargement of these organs. Some authors hold that the liver may be enlarged because of fatty infiltration, frequent gastrointestinal disorders and other diseases. The liver and spleen may descend as a result of deformation of the thorax. One of the reasons is apparently hyperemia of these organs. Normally contractions of the diaphragm help to move the blood from the liver to the inferior vena cava. If the muscular layer of the diaphragm contracts feebly, the blood becomes congested in the liver, and the latter enlarges and loses its significance as a blood depot.

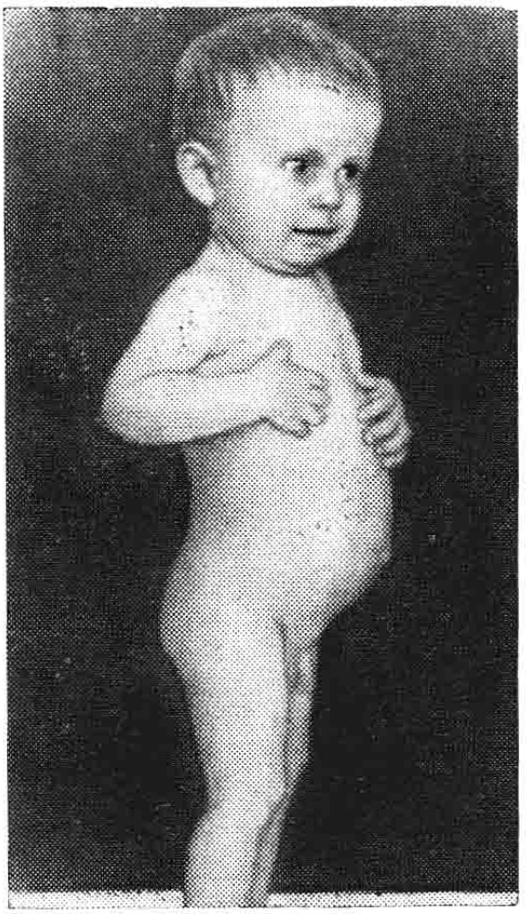

Fig. 4. Enlarged abdomen of a rachitic child

Dysfunctions of the digestive organs in rickets are manifested primarily in diminished appetite. The frequency of this symptom depends on the severity of the process. In first and second degree rickets anorexia is observed in 34-40 per cent of the children, in third degree rickets—in 56.5 per cent. Loss of appetite occurs particularly frequently in hypotrophic children. Poor appetite is observed in 15-17 per cent of normally nourished or slightly undernourished children affected with the same form of rickets; in second and third degree hypotrophy loss of appetite is noted in 45.8 and 80.7 per cent of the cases respectively.

Disturbed cortical regulation of the digestive processes is the primary cause of anorexia. Rachitic children show weakened functioning of the cerebral cortex, retarded reflex formation and predominance of processes of inhibition. Anorexia is manifested particularly sharply when the child's customary regimen has been altered, for example, on admission to children's institutions (nurseries, children's homes) during the period of adaptation to the new conditions.

Strong stimuli coming from the new external environment inhibit the activity of the cerebral cortex, and, if the diminished excitation involves the food analyser, the child's appetite deteriorates and the child develops a negative attitude to food (N. I. Krasnogorsky).

The loss of appetite caused by diminished secretion of gastric juice leads to disorders of the digestive processes. Secretory, absorptive and motor dysfunction of the gastrointestinal tract is observed. In rickets the total acidity of gastric juice may be from 4-6 to 10 and free acidity from 0 to 6-14 (K. P. Alexandrova). The activity of the enzymes (pepsin, lipase, etc.) considerably diminishes. Weakened activity of the secretory glands of the stomach affects the function of the pancreas because of the physiological unity between them. The phosphatase content in the intestinal mucosa and the excretion of the intestinal enzymes, especially phosphatase and saccharase, with the feces diminish (S. Y. Mikhlin), denoting dysfunction of the intestinal tract.

The hypofunction of the salivary glands observed in rickets, especially in cases involving dystrophy, also affects the normal process of digestion. As is well known, saliva participates in digestion in virtue of the enzyme—ptyalin—it contains. Absence of the requisite amount of saliva is responsible for dryness in the mouth which dulls the sense of taste and diminishes gastric secretion because it weakens the first complex-reflex phase of gastric secretion (P. D. Gorizontov).

Disturbances in the normal process of digestion are also dependent on changes in the functional state of the liver. Diminution of the glycogen-forming function of the liver has been demonstrated experimentally. Clinical observations have revealed changes in the antitoxic, urobilin and prothrombin-forming functions of the liver and in its ability to regulate the colloids of the blood serum. These disturbances are more strongly pronounced at the height of the rachitic process and less so during the period of reparation; however, in some children restoration of the hepatic functions lags behind clinical recovery (Y. M. Lukyanova). The functions of the liver are particularly disturbed in children with nutritional disorders. In dystrophy, even in its early stage, the carbohydrate, fatty, protein and pigment functions of the liver are altered and its barrier role is diminished.

The rachitic process is characterised by changes in the motor functions of the gastrointestinal tract. Peculiar gastric atonia with impeded evacuation and similar intestinal atonia with partial spasms of various portions of the intestinal tract are observed. The functional disorders of the gastrointestinal tract lead to frequent diarrhea. An unstable stool with undigested food particles, foamy and often containing light-yellow or in some cases grey and putrid mucus is observed in a considerable number of rachitic children. In addition to other factors, such a stool may be caused by deficiency of several vitamins.

Vitamin D deficiency leads to dyspepsia connected with impaired saponification of fats. Protracted diarrheas in rachitic children are apparently based on vitamin PP (nicotinic acid) deficiency. Prolonged enterocolitis-type diarrheas are observed in cases of vitamins B and A deficiency.

Hence, in addition to other factors, changes in the functions of the gastrointestinal tract are also connected with disturbances in the vitamin balance. On the other hand, the assimilation and utilisation of vitamins are

closely dependent on the functional state of the digestive organs. The liver cannot play the role of vitamins A and D depot in cases of deviation in fat metabolism, and carotene cannot be transformed into vitamin A. Sharp changes in fat metabolism during nutritional disorders are one of the causes of a graver course of rickets involving dystrophy. Diminished acidity of gastric juice, dysfunction of the intestines and deep disturbances in metabolism (mineral, protein, carbohydrate and fat) further aggravate the deficiency in vitamins which are extremely necessary for the growing organism of the child.

In rickets the dysfunction of the gastrointestinal tract facilitates attacks of acute diseases—dyspepsia and dysentery—which often affect children with rickets in the second or third stage. In these forms of rickets dysentery and dyspepsia exhibit marked clinical symptoms—toxicosis, protracted dysfunction of the gastrointestinal tract, and anorexia, and are complicated by pneumonia, otitis, pyuria, etc. These diseases may take a grave course with relapses and may become chronic (T. M. Zybina and M. N. Bessonova). Hence, rickets, especially at its height, involves marked functional and morphological changes in the most important systems of the organism, thus facilitating attacks of various diseases which, in their turn, aggravate the hypovitaminosis, acidosis and disturbances in all forms of metabolism. The occurrence and severity of diseases (infectious, gastrointestinal and respiratory) are also connected with diminished immunity. According to Y. F. Dombrovskaya, S. A. Bayandina and B. B. Krechmer, the phagocytic index and complement titer in rachitic children are diminished.

It is impossible to speak of the clinical and functional pathology of rickets without mentioning *anemia* which frequently occurs even during the incipient period of all forms of this process. A. B. Marfan and Bosányi believe anemia to be caused by changes in the bone marrow as a result of repeated stimulation of an infectious and toxic

character, which leads to hypofunction of the bone marrow and disturbance in hemopoiesis.

Other authors (Czerny, György) ascribe the development of anemia to acidosis. In acidosis the organism excretes an increased amount of ammonia which largely forms from histidine (amino acid) used in the synthesis of globin. In protracted acidosis the histidine required for normal erythropoiesis is destroyed, with anemia as a result.

The effective action of vitamin B_{12}, folic acid and pyridoxine (vitamin B_6) in the treatment of pernicious anemia (Aruffo, Stepantschitz, Schreiner, Mollin, Ross) attests the importance of these vitamins in the processes of normal hemopoiesis.

Vitamin C deficiency observed in rickets undoubtedly affects the processes of hemopoiesis, aggravating the disorders caused by this disease. It has been demonstrated clinically and experimentally that in cases of ascorbic acid deficiency there are marked changes in the erythrocytes and leukocytes. These changes involve stable hypochromic anemia of a hyporegenerative character, degenerative changes in erythrocytes—anisopoikilocytosis, and phenomena of beginning regeneration with an increase in young, immature forms in the blood—polychromatophils, normoblasts and reticulocytes. The number of leukocytes is diminished and neutrophilia with a shift to the left (to young forms), lymphocytosis and aneosinophilia are observed.

No paramount importance can apparently be attached to one or several causes in the development of anemia. Anemia is a pathological phenomenon which develops in rickets as a result of deep disturbances in the normal physiological state of all organs and systems of the organism. It is conditioned not only by rickets proper, but also by the defects in the care and nutrition of the child, which cause weakening of the regulatory role of the cortex in the process of hemopoiesis.

In rickets anemia is most frequently of a hypochromic character and is connected with defects in formation of hemoglobin. Severe forms of rickets exhibit not only diminished hemoglobin and erythrocytes, but also changes in their form and colour, and appearance of macronormoblasts. The picture of erythropoiesis shows depression of this process, on the one hand, and a pathological stimulation of bone marrow elements with signs of clearly marked degeneration, on the other hand (A. F. Tur, M. S. Osetrinkina, O. M. Lago).

The leukopoiesis is also altered. In some cases only a diminished function of the bone marrow as regards leukopoiesis is observed; this state is manifested in a slight and inconstant decrease in the leukocyte count in the peripheral blood (to 8,000-9,600). In other cases stimulation of leukopoiesis accompanied by an increased number of leukocytes (to 11,700-14,600) and clearly marked cell degeneration is observed. The number of neutrophils is increased with a shift to the left (appearance of young cells and increase in the number of band cells), the number of lymphocytes and monocytes is decreased, and in some cases aneosinophilia is observed. No interdependence between the intensity of anemia and the severity of the rachitic process has been established.

The changes in erythrocytes and leukocytes, denoting disturbances in the function of the hemopoietic organs, are more strongly pronounced in sharply undernourished children (second and third degree hypotrophy) and in all children at the height of the disease.

In rickets vitamin C deficiency is responsible for sharper disturbances in the functions of the hemopoietic organs since it produces degenerative changes in them. In cases of marked vitamin C deficiency (0.1-0.29 mg% in the blood) a sharp diminution of hemoglobin (to 52-55 per cent) in all children regardless of the severity of the rachitic process, and a decrease in the erythrocyte count (to 3,000,000-3,750,000) and in the colour index (to 0.62-0.65)

are observed, the number of leukocytes diminishes (to 7,200-5,400), the eosinophils disappear, the number of monocytes decreases, and moderate lymphocytosis with a slight shift of the neutrophils to the left appears.

In conclusion it may be said that the changes caused by vitamin D deficiency are the leading symptoms in the clinical picture of rickets in very young children. But the hypovitaminosis accompanying rickets in large measure determine the severity and course of the disease by deepening the metabolic disorders. That is why rickets can be considered a *hypovitaminosis.*

Rickets is characterised by a number of symptoms denoting *functional changes in the central and vegetative nervous systems.*

The character of sleep can be one of the most important characteristics of the child's psychoneurologic state. The sleep of healthy children is calm, deep and long. The process of inhibition operates normally and the children readily fall asleep. Rachitic children fall asleep with difficulty, cry out in sleep, readily awaken from light sounds, speech of adults and the crying of other children. Sleep disturbances are equally often (in 76-78 per cent of the cases) observed in all forms of rickets.

The development of speech in rachitic children lags. It has been established, by long observation, that only 30-40 per cent of the children with second degree rickets begin to speak at the age of 1 to 2 years, most of them uttering incomprehensible words without joining them in sentences. Children of the same age with third degree rickets lag still more in the development of speech. A 2- or 3-year-old healthy child freely speaks in complex sentences reflecting reality as it appears to his understanding and imagination. In severe forms of rickets the development of speech corresponds to the age level only in 22 per cent of the children of this age, while 63 per cent utter simple sentences and 15 per cent but separate words. If the child has nutritional disorders, the development of

speech is still more retarded. Even slight nutritional disorders affect speech, while deeper disorders impede the development of speech for a long time. However, such considerable backwardness in the development of the psychoneurologic activity of children cannot be accounted for only by the pathologic conditions produced by rickets, because training also plays an important part.

Rachitic children are inactive, lack initiative and take no lively interest in their surroundings. Irritability and monotonous crying are noted the more often, the more severe the rachitic process and the deeper the nutritional disorders. With such children it is difficult to make contact, evoke a smile or a lively reaction. It is generally known that children acquire a good deal of knowledge and many skills in play and that their psychoneurologic activity rapidly develops as a result of constant association with adults and other children.

Observations of rachitic children have shown that many of them cannot take part in the games and organised activities because they lack vigor owing to neuromuscular underdevelopment, react slowly, tire rapidly and in some cases fall asleep. At the height of the disease conditioned reflexes to stimuli of medium strength either completely fail to form or form after 8-61 combinations (in healthy children after 3-8 combinations) and cannot be consolidated. Even during convalescence, negative conditioned stimulation is followed by deep inhibition manifested in loss of the conditioned bond which is sometimes more difficult to restore than to form (T. T. Zaitseva-Gryaznova, 1955). Even so incontestably strong a stimulus as a toy fails to elicit positive emotions in such children. They do not take toys themselves and throw the toys away when they are placed in their hands.

But however deep the causes of disturbances in psychoneurologic activity in rickets, especially in cases combined with dystrophy, it is possible by a loving and considerate approach to children and well thought-out educational

measures, in addition to all other measures (proper care, regular and adequate diet, and appropriate medical treatment), quickly to do away with these deviations in the development of the children and to hasten their recovery.

It should be constantly borne in mind that, whereas prolonged disturbances in metabolism caused by some factors or others may result in retarded development of the functions of the central nervous system, the child's inactivity, sluggishness and poverty of emotions lead to decline of the basic physiological processes and cause diminished metabolism, undernourishment and trophic disorders. Only a unity of functional relations between the cerebral cortex and the internal organs conditions their adequate activity and ensures normal development and existence of the organism in the external environment.

CLASSIFICATION

For practical purposes it is very important to distinguish the various forms of rickets in young children. This is necessary to diagnose the disease correctly and to prescribe appropriate treatment. A single classification of rickets is required for a detailed and deep study of the disease. The use of a single classification by all the authors studying this question makes it possible to compare the results of examination of various contingents of children and to elaborate measures aimed at eradicating this disease.

In the Soviet Union the classification proposed by S. O. Dulitsky and adopted by the Sixth All-Union Congress of Pediatricians in 1947 is used.

Three degrees of rickets are distinguished according to this classification: first degree (mild), second degree (moderately severe) and third degree (severe); according to periods of the disease—initial, height of the disease, convalescence, and period of residual phenomena; according to its course—acute, subacute and relapsing.

In *first degree* rickets there are a few feebly marked symptoms on the part of the nervous and osseous systems.

Second degree rickets is characterised by moderate phenomena in the nervous, osseous, muscular and hemopoietic systems. The liver and spleen may be enlarged.

Three degree rickets differs from the two former forms by sharp changes in the nervous, osseous (deformities), muscular and hemopoietic systems accompanied by arrested physical and often mental development, undernourishment and acute anemia. Enlarged liver and spleen are common occurrences in this form of the disease.

The *initial* period which lasts 1-2 months, depending on the course of the disease (acute or subacute), is characterised by the following symptoms: restlessness, irritability, hyperhidrosis, occipital alopecia, moderate softening of the edges of the skull bones, incipient craniotabes and a small rosary. Biochemical analysis of the blood reveals a somewhat diminished amount of phosphorus; the calcium content is normal; the $\frac{Ca}{P}$ coefficient is increased. At this period roentgenograms may show no changes in the bones or show abnormal porosity and a slight fringiness of their ends.

At the *height* of the disease all the symptoms intensify. Skeletal deformities, muscular hypotonia, enlargement of the liver and spleen, anemia and disturbances in the static and motor functions are observed; retarded psychophysical development is more clearly marked.

The phosphorus and calcium content in the blood decreases and the $\frac{Ca}{P}$ coefficient diminishes.

Bone roentgenograms show definite changes—the contours are slurred, the ends of bones are goblet-shaped, the edges of the metaphyses are fringy and indistinctly outlined.

The *convalescence* period is characterised by retrogression of the symptoms of rickets. The edges of the cranial

bones grow more compact, which is particularly clearly seen at the anterior fontanel, craniotabes diminishes and disappears, teeth erupt and the static and motor functions are restored. The general condition of the child improves.

The amount of inorganic phosphorus in the blood increases, while that of calcium may remain below normal; the $\frac{Ca}{P}$ coefficient diminishes. Roentgenograms show a reparative zone in the form of a dark band in the region of the metaphysis. The cortical layer of the bone expands.

The period of *residual* phenomena corresponds to the end of the rachitic process. The residual phenomena may be bone deformities, changes in the teeth and anemia. Any of these phenomena attest that the child has survived a severe attack of rickets (second or third degree).

In cases of *acute* rickets all the symptoms develop very rapidly. The first symptoms are observed in the nervous system (restlessness, hidrosis) and the bones (softening of the edges of the cranial bones, especially at the fontanels). Acute rickets is most frequently observed in infants (in the first months of life) and is particularly characteristic of prematurely born children.

The *subacute* course of the disease is characterised by a slow development of the rachitic process. In such cases phenomena of osteoid hyperplasia predominate in the osseous system (rosary, bosselated cranial eminences, thickening of the epiphyses of tubular bones). In children with nutritional disorders softening of the bones may be observed in addition to osteoid hyperplasia. Rickets most frequently runs a subacute course when it develops against the background of dystrophy and when it occurs in older children.

In *relapsing* rickets periods of improvement are followed by aggravations of the rachitic process under the influence of unfavourable external environment.

Such a course of rickets is observed in children fre-

quently affected with acute or chronic diseases. Treatment discontinued too soon may also lead to a flare-up of already extinguished symptoms of rickets.

In diagnosing rickets in a child and establishing its severity, period and course, the physician must take into account the child's age, state of nutrition and diseases suffered by the child in the past. Without taking these circumstances into consideration it is easy to make a mistake.

Even when the symptoms of the different periods of the rachitic process indicated in the classification are taken into account it is sometimes difficult clinically to establish the transition from the height of the disease to the period of convalescence and from the latter to that of residual phenomena without long observation of the child. And then too the physician is largely subjective in evaluating the child's condition. The biochemical indices in chronic nutritional disorders, even during the period of residual phenomena, may be altered and characteristic of the height of rickets or the period of convalescence. Roentgenograms of the epi- and metaphyseal ends of bones furnish the most objective data.

According to S. O. Dulitsky, acute rickets is characteristic, as was already mentioned, of children in the first months of life. However, a rapid development of the rachitic process is sometimes also observed in older children, when the disease sets in against the background of diminished reactivity of the child's organism following an attack of a severe disease or a sharp change in the external environment.

Changes in the vegetative nervous system occur not only in acute rickets. Very often sweating and other signs of disturbances in vegetative regulation are observed in children affected with the second or third degree rickets with clear symptoms of osteoid hyperplasia which, according to the classification, are characteristic of subacute rickets. These possibilities must be taken into account when any particular case of rickets is considered.

In infants rickets does not always run the same course. A number of circumstances may sharply alter its clinical picture and course. Rickets is aggravated and complicated by respiratory, gastrointestinal and infectious diseases, irrational feeding, failure to observe a hygienic regimen and other unfavourable factors of the external environment.

Rickets with intestinal infantilism (celiac disease), a relatively rare disease, is closely connected with deep disturbances in mineral metabolism caused by severe digestive disorders and dysfunction of the endocrine glands. "Intestinal" rickets exhibits retarded growth which leads to a state of dystrophic subnanism (Y. F. Dombrovskaya). Such patients have a negative phosphorus and, especially, calcium balance. A definite ratio of the calcium compounds to the fats in the food (0.04-0.08 g of calcium per 1 g of fat) is a matter of necessity. Children affected with the celiac disease do not assimilate the fat consumed with the food and a large amount of fatty acids accumulates in the gastrointestinal tract. As a result calcium carbonates and phosphates are bound by the afore-mentioned acids and, failing to be absorbed, are excreted from the organism because the intestines lack the bile acids needed to change the large amount of calcium soaps formed in the intestines to a soluble state. Hypophosphatemia and hypocalcemia are constant concomitants of this state. Roentgenograms show typical rachitic changes and considerable osteoporosis. According to Y. M. Lepsky, it is difficult to explain the appearance of rachitic changes proper only by poor absorption and the resultant inadequate supply of vitamin D with the food. Ultraviolet irradiation in this form of rickets proves in most cases ineffective.

This severe affection is apparently caused not only by vitamin D deficiency and disturbance in mineral metabolism, but also by changes in hormonal and enzymatic functions of the organism and very deep disturbances in

the intermediate metabolism of all substances. Increased excretion of unassimilated most important nutrient substances, mineral salts and vitamins results in development of dystrophy and hypovitaminosis. These factors determine the severe course of so-called intestinal rickets which is not amenable to usual anti-rachitic treatment.

Late rickets is a connecting link between rickets of early childhood and osteomalacia of adults. On the other hand, the wartime spread of rickets typical of early childhood to the older age group brings the latter closer to late rickets.

Most authors hold that late rickets appears in children past 4-5 years of age, most frequently between 8 and 12. Late rickets may run a protracted course. In some cases it is a rachitic process persisting since early childhood and intensifying towards the time of sexual maturation, in others it is a disease appearing for the first time at pre-school or school age. Children begin to complain of pains in the back, the knee joints and feet, the pains increasing during physical effort. Long standing and walking are difficult. Sometimes such children waddle.

True late rickets (according to Marfan) is manifested in two forms. The severe form of the disease is characterised by generalised deformities of different intensity affecting the upper and lower extremities, the ribs and even the skull. In milder cases the deformities are limited to moderate scoliosis, kyphosis, lordosis, coxa vara, genu valgum, genu varum and pes planus. Such deformities observed in children of school age may be considered manifestations of late rickets. In the latter form the changes are localised in the lower limbs, the upper limbs are involved sometimes, the thorax is affected extremely rarely and the skull never. In cases of severe and prolonged rickets the growth may be arrested to the point of nanism.

The descriptions of other symptoms of late rickets by different authors are contradictory. Y. M. Lepsky holds

that the symptoms of early rickets, connected with such disturbances in the nervous system as irritability and sweating, as well as muscular hypotonia and weakness of the ligamentous apparatus, are very rarely observed in late rickets. The liver and spleen are not enlarged. Others find that this disease is connected with marked vegetative-endocrine disorders (functional cardiovascular disturbances, increased or diminished gastric juice acidity, enteroptosis, hyperthyroidism, acrocyanosis and hidrosis). All the peripheral lymph nodes, the spleen and liver are enlarged. The children are irritable, psychically unstable and often inhibited. Disturbances in the mineral balance and rachitic changes in the osseous system are in such cases apparently connected not only with vitamin D deficiency or inadequate effect of ultraviolet rays, but also with endocrine disorders (including the gonads) hypovitaminosis and the patient's diet (Y. F. Dombrovskaya).

In late rickets, as in rickets of early childhood, diminished phosphorus and calcium in the blood are observed, hypophosphatemia being the more constant symptom and persisting longer after clinical improvement (Holt). The alkaline reserve is decreased to 37.7 vol.% CO_2 (R. M. Muravina) as against the 53.5 vol.% in healthy children. Changes in protein and carbohydrate metabolism have also been found. Roentgenography is the most reliable diagnostic method since it shows changes in the meta- and epiphyseal parts of the bones most characteristic of the rachitic process. Some cases reveal considerable osteoporosis to which fractures, infractions and angulations of bones in severe forms of late rickets are ascribed. Special changes in bony tissue—reorganisation zones—are sometimes observed (D. Y. Kuzmin, Looser).

Mild cases of late rickets are more amenable to treatment with vitamin D. According to Carlgren, Gregersen, and Holt, administration of large doses positively affects mineral metabolism, increases the activity of alkaline phosphatase, improves the roentgenographic data and

gradually leads to recovery. In severe cases involving generalised deformities in the osseous system and endocrine hypofunction even massive doses of vitamin D prove ineffective. In such cases it is necessary to give the patients general roborant treatment and administer endocrine preparations and orthopedic aid.

Renal rickets occurs rarely. This disease is characterised by a combination of bone lesions (disturbances in their growth and development) with functional chronic renal insufficiency as a result of interstitial nephritis or defective development of the urinary system.

The connection between the process in the bones and renal disease was first established by Marley and Fletcher in 1911 (quoted from Welz). They named this disease *renal infantilism*. Changes in the bones characteristic of rickets and found in this disease justified a number of authors in regarding it as *renal rickets*.

Other authors found only rachitic changes differing from true rickets and therefore considered this form of disease a *pseudorickets* or *renal nanism*.

The pathogenic connection between chronic renal disease and rachitic changes in the bones is still unclear. Mitchell holds that the diminished excretion of phosphates in the urine observed in renal rickets leads to hyperphosphatemia and increased excretion of phosphates into the intestines where they form with calcium sparely soluble compounds which are not absorbed but are excreted with the intestinal contents. Deposition of salts in the bones is also hampered by acidosis resulting from disturbances in the excretory function of the kidneys. Recent studies (Rupp, Swoboda, 1954) of renal functions by intravenous administration of PO_4 have established diminished tubular reabsorption of phosphates in late rickets connected with renal disease.

Changes in the bones in renal rickets are ascribed to secondary hypertrophy of the parathyroids as a result of protracted renal disease (A. V. Rusakov) or to a lesion

in the brain and the hypophysis (Debré et al). The participation of endocrine glands in the process may account for the nanism always observed in these cases. Many authors hold that there is no vitamin D deficiency in renal rickets because anti-rachitic therapy involving administration of this vitamin aggravates the affection.

Manifestations of renal rickets begin at preschool and school, and sometimes at an earlier age. In some cases the onset of the disease is manifested by polydipsia and polyuria. The low specific gravity of the urine at this period may lead to erroneous diagnosis of diabetes insipidus. The patient's skin not infrequently assumes a greyish-yellowish coloration. Gradually changes in the heart develop and the arterial pressure rises. Renal insufficiency leads to metabolic disturbances and acidosis develops. The phosphorus in the blood sharply increases—to 20 times the normal amount (Welz). Sometimes the calcium content diminishes, in other cases it remains within normal limits or increases. Protein metabolism is altered and accumulation of residual nitrogen in the blood is observed. Cholesterol increases to 500%. Hypochromic anemia appears.

Rachitic changes develop slowly. The epiphyses of the long bones of the limbs thicken in the form of bracelets and the rosary grows very large. The thorax becomes deformed (eversion of the lower aperture and compression from the sides) and kyphosis, lordosis, scoliosis and curvature of the shanks are noted. Myopathy and excessive stretching of the ligamentous apparatus may be observed. Locomotion becomes increasingly difficult and the patients cease to walk. Growth and development become more and more retarded. A 7-year-old child may have the weight and height of a 1-year-old infant (A. I. Gingold, V. P. Oranskaya), while 16-18-year-olds may look like 10-12-year-old children.

Roentgenography of the bones establishes changes characteristic of far advanced rickets, but with marked dys-

trophic phenomena and extreme osteoporosis. As distinct from primary rickets, fibrous tissue develops in the bone marrow cavities (A. N. Koltover).

Recovery from rickets connected with chronic renal insufficiency is observed very rarely. Anti-rachitic therapy is ineffective. The patients die of uremia sometimes within a few years of the onset of the disease.

CHANGES IN THE OSSEOUS SYSTEM AS REVEALED BY ROENTGENOGRAPHY

Bones are very sensitive to all pathological phenomena in the organism. In infectious process, metabolic disorders, vitamin deficiency, incretory correlation (enzymatic and hormonal) or affections of the nervous and muscular systems careful study reveals reactions of the osseous system. Like all tissues in the organism, bony tissue is always in a dynamic state. Two antagonistic processes—anabolism and catabolism—operate in the bones all through life.

Constant renewal is the peculiar property of bone. The natural processes operate with a definite equilibrium subject to the influence of regulatory mechanisms and are maintained by a number of systems which form intermediate links in this regulation.

Many parts of the bony skeleton are affected in rickets. Changes in the bones of the cranial vault, on the ribs and the long bones of the limbs are most frequently observed. The bones in the zones of growth are affected the most—at the junctions of the diaphysis and epiphysis, and at the end of the diaphysis of long bones, inside and around the ossification nuclei of the short and the epyphyses of the long bones, under the periosteum of flat bones, especially where the process of ossification is more active at the moment of the onset of rickets.

In fresh cases of rickets the bones are lighter than normal, are soft and bend easily. This is due to the greater water content and lesser amount of mineral substances. The following is the composition of a normal and a rachitic rib cited by way of illustration (from I. A. Shabad).

	Normal rib (in%)	Rachitic rib (in%)
Water	14.4—32.9	42.4—66.4
Organic substances	26.9—39.1	20.7—27.4
Ash	40.2—46.6	7.9—32.0
CaO	21.7—25.3	4.2—16.8
P_2O_5	12.3—18.9	3.3—12.8

Macroscopic examination of the junctions of the diaphysis and epiphysis of bones reveals hyperemia and a thickening; similar changes can also be observed under the periosteum. Microscopically the pathological phenomena are most strongly pronounced at the sites of bone growth—at the junctions of the cartilage and bone and in the region of the periosteum.

In normally growing bone the line of ossification at the junction of the bone and cartilage is even and smooth and separates the granulation layer of the bone (rich in blood vessels) from the epiphyseal cartilage.

The strip of cartilage closer to the ossification line consists of two layers: a dull white and yellowish regressive layer of cartilage with layers of calcium (preparatory calcification zone) and a bluish proliferative layer, the site of multiplication of cells which lie in rows parallel to the longitudinal axis of the bone. Capillaries surrounded by bone marrow cells come up to the cartilage from the direction of the diaphysis. The capsules of the cartilage cells dissolve on contact with the capillaries and the liberated cells find themselves in the bone marrow. Osteoblasts arrange themselves on the surface of the cartilagi-

nous septa which grow over with an osteoid layer; in normal bone this layer is quickly impregnated with salts and is transformed into bony tissue. It follows that the septa of the basic substance of the cartilage serve for the construction of the trabecula of the spongy part of the bone around which various bone marrow cells arrange themselves.

In the rachitic process the proliferative layer of the cartilage considerably thickens. The granulation tissue of the bone penetrates together with the capillaries deep into the proliferative layer, for which reason the smooth, even line which in normal bone separates the epiphyseal cartilage from the bony tissue of the diaphysis becomes irregular, wavy and crenated. No calcium salts are deposited in the newly formed osteoid tissue or only separate sections impregnated with them are observed. Some cartilage cells are transformed into bone by direct metaplasia. The newly forming irregularly shaped bone trabeculae are covered with a wide layer of osteoid tissue which is not impregnated with mineral salts and the growth of bone is deranged.

As a result of all these changes an abnormal rachitic zone 1-2 mm thick is formed; it consists of various and disorderly arranged elements—cartilage cells forming columns or isles, blood vessels surrounded by connective tissue, trabeculae of osteoid tissue and stellate and spindle-shaped bone marrow cells originating in the perichondrium surrounding the blood vessels. In severe cases of rickets the normal bone marrow may be in large measure replaced by such cells, which may constitute one of the causes of anemia accompanying the main process.

In bones developing from a connective tissue base, such as the skull bones, the changes are essentially the same as those described above, but since the normal process of bone resorption continues and even intensifies, the flat bones of the skull readily soften (craniotabes), other bones grow thinner (in the previously formed parts) and

thicker at the sites of intensively forming osteoid, non-calcifying tissue.

Hence, in rickets the changes in the bones proceed in three directions: 1) osteoid hyperplasia, i.e., excessive growth of the osteoid tissue leading to development of bosselated cranial eminences, rosaries, and bracelets in the region of the epiphyses of the upper and lower limbs; 2) hypogenesis—inadequate bone development which retards the growth of the bones in length; 3) osteomalacia —demineralisation, increased resorption which causes softening of the already formed bones and facilitates deformation of the skeleton (skull, thorax and limbs) and bone fractures.

Roentgenography is one of the objective methods of diagnosing rickets. According to some authors (S. A. Reinberg, V. A. Dyachenko, G. I. Kharmadaryan, M. M. Raits, Wimberger and Göttche), however, there is no early roentgen diagnosis of rickets. With such clinical signs characteristic of the initial stage of first degree rickets as foci of cranial bone softening, craniotabes and rosary, it is as yet not always possible to establish clear changes in the osseous system by roentgenography. In addition to clinical data, changes in the phosphorus and calcium metabolism are the more reliable diagnostic symptom during this period. At later periods in the development of the rachitic process roentgenography furnishes a complete pathoanatomical, or even pathohistological, picture of the changes in the bones, the severity of the disease and its period, and in many cases establishes the end of the reparative process more clearly than do clinical examinations and biochemical studies.

In rickets the most characteristic picture from the standpoint of roentgenology is one that shows pathological changes in the region of the epiphyses. A roentgenogram of the radiocarpal joints suffices to determine the existing changes since the forearm bones are affected by rachitic

changes first (or, at any rate, simultaneously with the cartilaginous ends of the middle ribs).

Disturbances in mineral metabolism lead to calcium deficiency in the bones, which is roentgenographically evident in general osteoporosis and little contrast.

At the early stages of the disease the preparatory calcification zone begins to assume the appearance of a horizontal band, instead of the normally convex one. A slight loosening of the zone, especially in its middle, may be observed with separate small clarifying foci appearing in the dark band (Figs. 5 and 6).

At the height of rickets the dark band disappears altogether, the normal boundary between the epiphyseal cartilage and metaphyseal spongy substance no longer exists, and the metaphyseal spicules end freely in the direction of the epiphyses in the shape of hairs, tassel or uneven fringe. Instead of the normal narrow and light band—projection of the epiphyseal cartilaginous disk—a wide epiphyseal clearing of the rachitic zone appears. In a number of cases the metaphysis increases in diameter and assumes the characteristic form of a saucer or goblet (Figs. 7 and 8).

The anatomical basis for the goblet-shaped deformation of the metaphysis of bones is an enlarged rachitic zone (intensive growth of osteoid tissue). These changes become visible only after appearance of the zone of preparatory calcification of the bone edges. Recovery in cases of saucer-shaped changes in the diaphyses begins with a deepening (resorption of the spongy tissue), which, if the reparative process runs a favourable course, is subsequently filled with calcium, and the epiphysis gradually assumes its normal shape (Göttche) (Fig. 9).

The epiphyseal ossification points show the same changes as are discovered in the metaphyses. The nuclear shadow is barely seen in the roentgenogram. The contours of the nucleus are uneven, especially on the side facing the epiphyseal cartilage zone.

The basal zone corresponding to the preparatory calcification belt is absent. In rickets the ossification points appear in time, although in the roentgenograms they seem to be late. In severe cases of rickets the nuclear shadow disappears altogether. The ossification points of the distal epiphysis of the radius and of the bones of the radiocarpal joint serve as the most precise identification in rickets. In healthy children ossification points usually appear at the age of 3-4 and not later than 6 months, first in the capitate and then the unciform bone. The ossification nucleus in the distal epiphysis of the radial bone emerges in the beginning of the second year (D. G. Rokhlin).

The roentgen signs of diaphyseal changes in severe forms of rickets are less clear. The compact cortical substance grows thinner and the contours of the cortical layer, especially on the outside, become blurred and unclearly circumscribed. Longitudinal lamination corresponding to separation of individual bony plates appears (S. A. Reinberg).

Undernourished children show roentgenographically fewer marked bony changes in severe forms of rickets than normally nourished children do in milder forms of the disease. Thus in severe cases of rickets roentgenography alone does not permit of diagnosing the disease and determining its severity. The conclusion can be drawn only by considering the entire clinical picture, the state of the child's nutrition and the biochemical indices of phosphorus and calcium metabolism (Figs. 10 and 11).

In rickets true fractures occur extremely seldom. Roentgenograms sometimes show angulations and infractions (of the greenstick-fracture type), i.e., partial transverse subperiosteal infractions of the cortical substance with an angular displacement seen on the concave side of the curved bone. Zones of bone reorganisation appearing in severe cases of rickets are often mistaken for fractures. Bone reorganisation constitutes a peculiar acute transformation process attesting special biological mobility of

bony tissue as a result of altered conditions (pressure against the softened bone, muscular hypotonia, change in the traction of different muscle groups, altered point of greatest stress). Roentgenographically the reorganisation zones appear as clear bone defects running through the entire thickness of the diaphysis, transversely or obliquely, with periosteal stratification greatly resembling calluses. Reorganisation zones are most frequently found in the ulna, fibula, more seldom in the radius, and extremely rarely in other bones (V. A. Dyachenko, D. Y. Kuzmin and M. M. Raits).

Clinically the reorganisation zones are not easy to find. Even when these zones are clearly marked in roentgenograms, the pain on palpation is slight and is not strictly localised.

During the Great Patriotic War some Leningrad children exhibited diseases attended with skeletal affections not entirely characteristic of rickets. Skeletal deformities and arrested growth came to the foreground. According to A. F. Tur and E. I. Fridman, these changes in the osseous system were a manifestation of dimineralisation caused by vitamins D and C deficiency. In these cases roentgenographic symptoms of rachitic bone affection were either absent or negligible.

There is no early diagnosis of osseous changes caused by ascorbic acid deficiency in the organism. Distinct changes in the bones are found only in far advanced cases when the clinical picture is so clear that it requires no roentgenographic confirmation. In cases of vitamin C deficiency combined with rickets the latter can be found roentgenographically only in its severe forms (Bromer, Harvey).

In cases of mild symptoms of vitamin C deficiency roentgenograms show a normal picture or a certain measure of osteoporosis without any other characteristic signs. Sometimes it is possible to see a small clearing in the subchondral zone of the metaphysis, which is the result

of disappearance of some of the bony trabeculae. But similar changes are also observed in the initial stages of rickets and therefore when rachitic children in whom, moreover, vitamin C deficiency has been established biochemically, are roentgenographed, it is difficult to decide whether the aforesaid changes are a result of vitamin C deficiency or of rickets. In such cases the clinical picture and determination of phosphorus and calcium in the blood assume paramount importance.

M. V. Maretskaya's observations (1943-45) established that children with chronic nutritional disorders may develop general systemic osteoporosis, which she described as osteopathia, rather than true rickets. The clearest sign of osteopathia is retarded growth as a manifestation of atrophy of bony tissue. Roentgenography shows delayed appearance of ossification nuclei in the epiphyses with a clearly contoured growth zone and normal epiphyseal outlines. Characteristic of osteopathia are frequent fractures with displacement of the fragments, unlike the greenstick fractures (observed in rickets), due to extreme thinning of the cortical layer of the diaphyses. A thinning of the cortical layer and rarefaction of the bony structure, most clearly manifested in the metaphyses, as well as absence of ossification nuclei in the bones of the limbs, have also been established roentgenographically in experiments on young animals in which alimentary dystrophy was produced.

Many of these symptoms are, as was already mentioned, also characteristic of rickets (delayed appearance of ossification nuclei, thinning of the cortical layer of the diaphysis, rarefaction of the bony substance of the metaphysis, etc.), but in rickets a disturbance in the zone of preparatory calcification and changes in the outlines of the epi- and metaphyseal parts of the bones are observed.

The healing of rachitic lesions of the osseous system begins with deposition of calcium salts in the growing bones. A new zone of preparatory calcification appears in

place of enchondral ossification. It appears as a dark, uneven, arciform band in the middle of the light rachitic zone and closer to the articular end of the bone rather than at the end of the ossified metaphysis. The newly appeared calcification zone separates the osteoid metaphyseal substance from the cartilaginous zone. Subsequently, if the process runs a favourable course, the calcification zone extends in the direction of the metaphysis until it completely merges with its spongy structure and all of the osteoid substance is impregnated with calcium. A wide, dark band of preparatory calcification appears in the roentgenogram.

In cases of relapse of the rachitic process a loosening appears in this zone and the band moves towards the metaphysis. Further calcification ceases and a new light band of osteoid substance appears parallel to the dark zone.

If calcium is deposited in the periosteal osteoid substance, longitudinal shadows adjacent to the cortical layer of the bone appear in the roentgenograms. Periosteal calcification shows that the rachitic process is assuming a reparative character (Fig. 12).

If the process improves, a calcification zone also appears around the epiphyseal ossification nucleus and calcium is deposited in the osteoid tissue. As a result, the ossification nucleus which was vaguely outlined or entirely invisible in the roentgenogram reappears and assumes normal shape.

Roentgenography makes it possible to establish a definite dependence of the intensity of the bony changes on the severity and period of the rachitic process. At the height of first degree rickets a change in the zone of preparatory calcification (loosening, slurring, fragmentation) can be discovered. In single cases the distal ends of the forearm bones are everted. The cortical layer of the diaphyses and the contours of the ossification nuclei are quite frequently slurred, which denotes osteoporosis.

In second degree rickets the bone changes pathognomonic of the given process are much more strongly pronounced. According to the author, looseness and fragmentation of the zone of preparatory calcification are found in 90-92 per cent of the cases, complete resorption—in 5-7 per cent, eversion of the epi- and metaphyses—in 56.7 per cent, goblet-shaped metaphyses—in 10-11 per cent and marked stratification of the cortical layer of the diaphysis—in 74-75 per cent.

Phenomena of osteoporosis in moderately severe and severe forms of rickets are observed more frequently and are more strongly pronounced. A slurred picture of the bones, an indistinctness and diffusiveness of the cortical layer and the contours of ossification nuclei are observed in 74-76 per cent of the cases, total disappearance and seemingly late appearance of ossification nuclei—in 19-20 per cent. Bone fractures or, to be exact, infractions of bones at the junction of the metaphysis and diaphysis are not noted so often; according to the author's observations, they are found in 1.5-3 per cent of the rachitic children at the height of second and third degree rickets.

According to some authors, no rachitic changes are found in children with chronic nutritional disorders either by clinical examination or roentgenography. During the Great Patriotic War it was observed that severe forms of rickets developed in cases of dystrophy and that the severity of the process ran parallel to the extent of nutritional disorders (Y. F. Dombrovskaya, A. F. Tur, M. M. Pikkel et al).

According to the data at the author's disposal, considerable changes in the bones, established roentgenographically, are found in rickets against the background of dystrophy. But not all symptoms occur with equal frequency. Disturbances in bones caused by the process of decalcification (slurring and disappearance of the preparatory calcification zone, erosion of the cortical layer of the diaphyses and contours of ossification nuclei, indistinct out-

lines of the bones) are more strongly pronounced in children with chronic nutritional disorders than in normally nourished children. Changes resulting from hyperplasia of osteoid tissue (expansion of the epi- and metaphyses, goblet shape) occur more frequently in normally nourished children and are observed much more seldom in marked nutritional disorders (second and third degree hypotrophy). This warrants the conclusion that children with chronic nutritional disorders exhibit symptoms typical of rickets, i.e., changes in the epi- and metaphyseal zone and the cortical layer of the diaphyses.

Considerable dystrophic changes in the bones occurring in rickets developing against the background of dystrophy are in large measure the result of vitamin C deficiency observed when these two morbid conditions are combined. Ascorbic acid is the regulator of osteogenesis ensuring differentiation of mesenchymal cells into osteoblasts and their secretion of the principal bony substance. Its deficiency in the organism disturbs the formation of osteoblasts and the bony trabeculae disapper, while the function of osteoclasts continues with osteoporosis and bone fragility as a result (V. N. Bukin, V. V. Yefremov, Rosenberg).

Graver rachitic changes in the bones are found roentgenographically in rachitic children with a low ascorbic acid level in the blood (0.1-0.2 mg%). Looseness, slurring and fragmentation of the preparatory calcification zone are observed in 88.1 per cent of the patients, total disappearance of this zone and the "tassel" symptom in 11.9 per cent, a slurring of the cortical layer of the diaphyses and contours of the nuclei in 95.2 per cent, late appearance of ossification nuclei in 26.2 per cent, marked osteoporosis in 97.6 per cent and greenstick fractures of the forearm bones in 2 per cent. But in addition to this some children have slightly expanded epi- and metaphyses (33 per cent) and goblet-shaped metaphyses (9.5 per cent) (M. N. Bessonova). Thus in cases of a low vitamin C level those bony

changes are more strongly pronounced which appear as a result of intensified processes of decalcification, resorption and hypogenesis.

Establishment of a correspondence between the clinical and roentgenographic pictures of bony changes in rickets is not only of theoretical, but also of practical importance. It would seem that a definite clinical picture with clearly marked bone symptoms must correspond to definite changes in the bones established roentgenographically. Observations of many authors do not confirm this. In the early stages of the disease roentgen pictures of children with clear clinical signs of rickets in the first year of life show very slight changes or no changes at all in the distal ends of the forearm bones. In a large percentage of cases the clinical and roentgenographic data do not coincide as regards evaluation of the phase of the disease. Rickets at its height may be established clinically, while roentgenography shows either the beginning of reparation or even complete restoration (N. A. Panov and Y. I. Kartsovnik, S. O. Dulitsky, E. I. Fridman). According to the author's observations, while roentgenograms show only a loosening and fragmentation of the preparatory calcification zone and loss of the convex form of the metaphysis, clinical manifestations are quite diverse. Craniotabes is found in 23.3 per cent of the cases, bosselated cranial eminences in 85.9 per cent, rosaries in 95.8 per cent, thickened epiphyses in 23.4 per cent, and thoracic changes in 76.5 per cent. Slurring, fragmentation and resorption of the preparatory calcification zone, distention and expansion of the epi- and metaphyses of the bones, indistinctness and longitudinal striation of the cortical layer are roentgenographically observed in second and third degree rickets, clinical symptoms being more numerous and more strongly pronounced. Bosselated cranial eminences are found in 93.1 per cent of the children, rosaries—in all children; epiphyseal thickenings (bracelets) on the upper and lower limbs are observed in 40 per cent of the patients, severe

deformities of the thorax (compression from the sides, transverse constriction, eversion of the lower edges) and lower limbs—in the overwhelming majority of the children.

In evaluating the phase of the disease by comparing the clinical and roentgenographic data the author found disparities in 10-12 per cent of the cases. With the clinical picture corresponding to the height of the disease roentgenography in some cases showed the initial period and in others the restorative phase. Complete disparity between the results of the clinical examinations and roentgenography was noted in most of the cases in infants with first degree rickets. Thus, according to A. M. Khvul, in 3- to 6-months-old children with a clearly marked clinical picture and biochemical indices denoting disturbances in phosphorus and calcium metabolism the diagnosis of rickets was not confirmed roentgenographically.

After treatment restoration of the normal bone structure goes through definite phases, yet the time required for this process to terminate is determined not only by the method of treatment but primarily by the child's condition, the reactivity of its organism, the severity and phase of the rachitic process, and the child's environment.

In cases of administration of large doses of vitamin D_2 (up to 100,000 u for a period of 6 days) a considerable effect is observed in normally nourished or slightly undernourished children. The reparative process is roentgenographically observed to appear 7-10 days after the beginning of vitamin administration. An ossification zone in the metaphyses of the bones becomes outlined in cases in which it was completely resorbed before treatment, while if the zone was eroded and fragmented before the treatment the bones become more compact; the goblets are filled in and the osteoporosis diminishes. All normally nourished children are cured within 8-9 weeks, which is confirmed roentgenographically.

The severity of the disease in similarly nourished children in some measure determines the course of the reparative process. In normally nourished children with first degree rickets marked reparation is observed within 5-6 weeks, in patients with second degree rickets—within 7-8 weeks. The effectiveness of vitamin D therapy also largely depends on the phase of the disease at the time of the beginning of treatment; in convalescent children this therapy is an impetus that accelerates the healing. In rickets combined with second and third degree hypotrophy administration of large doses of vitamin D_2 is scarcely effective and, although some positive changes are observed, these changes are not so significant and become apparent later. Phenomena of clearly marked reparation are noted only within 2-2.5 months, while the bones are normalised only within 3-4 months and sometimes later.

In most cases clinical improvement proceeds parallel to changes established roentgenographically. Sometimes roentgenographic data do not correspond to the clinical improvement in the rachitic process and very rarely roentgenographically discovered improvement precedes clinical improvement.

In children with marked vitamin C deficiency, hypocalcemia and hypophosphatemia, and, consequently, marked osteoporosis before treatment the process of reparation operates more slowly than in cases of a higher ascorbic acid level in the blood and better mineral metabolism indices. The author has found ascorbic acid to exert a positive influence on the course of the reparative process in rickets. One month after the beginning of vitamin C administration per os in a dose of 100 mg per day the zone of preparatory calcification begins to grow compact in 90.6 per cent of the children with second and third degree rickets, the cortical layer becomes more distinct, and ossification nuclei appear in the roentgenograms in 77.3 per cent, the osteoporosis diminishes and disappears in 80 per cent of the cases.

Treatment of children with severe forms of rickets involving second degree hypotrophy only with vitamin D_2 proves ineffective or of little effect in most cases (only very slight changes are observed roentgenographically).

In cases of administration of vitamin D_2 together with ascorbic acid and thiamine positive changes, namely, greater compactness of the preparatory calcification zone are observed within 3-4 weeks in 87 per cent of the children, a more distinct cortical layer of the diaphyses and more ossification nuclei in 78.5 per cent, and diminished osteoporosis in 70 per cent; only in 10 per cent of the cases do the changes appear later, i.e., with improvement of the child's nutritional status and normalisation of the stool.

Intercurrent diseases (influenza, chicken-pox, whooping-cough, pneumonia, gastrointestinal diseases) considerably diminish the effectiveness of treatment with vitamin D_2, as well as with its combination with ascorbic acid and thiamine, and in some cases aggravate the course of rickets, which is confirmed clinically and roentgenographically. However, it is necessary to administer vitamin D (in large doses), ascorbic acid and thiamine also in these cases because this mitigates the course of all intercurrent diseases by improving the rachitic process.

DIFFERENTIAL DIAGNOSIS

Early diagnosis of rickets is a *sine qua non* for the effective treatment of this disease. In day-to-day practice rickets is diagnosed on the basis of clearly visible skeletal changes, i.e., disorders which are a result of an already prolonged course of the disease. To find the earliest signs of this disease (before the appearance of bony changes), attention must primarily be devoted to functional disturbances in the nervous system (restlessness, irritability, poor sleep, excessive sweating, etc.). Changes in the osseous system appear 2-3 weeks after disturbances in the child's general condition are observed. But in order not to overlook the first bony changes one must watch for softenings of the flat bones of the skull at the edges of a fontanel, along the cranial sutures and on the squama occipitalis.

At this period the diagnosis may be confirmed by biochemical findings. Acidosis with diminished reserve alkalinity is a constant symptom of rickets even in its early stage. In healthy children the reserve alkalinity index is 55 per cent by volume; in rickets it drops to 31-43 per cent by volume (E. A. Reikher and co-authors, K. A. Svyatkina et al).

It is also important to determine the activity of the carbonic anhydrase which increases as a result of diminished oxidative processes in rickets. Normally the activity index is close to 1.0, in rickets it is between 1.4 and

2.0 (Y. F. Dombrovskaya and Y. M. Valter, T. I. Garsevanishvili).

Hypophosphatemia accompanies rickets in almost all cases. Even at the initial period the amount of phosphorus in the blood is between 3-4 mg% in 83.6 per cent of the children. Diminished reabsorption of phosphates in the renal tubules, leading to phosphorus metabolism disorders in the very beginning of the disease, is also a constant sign of the disease (K. A. Svyatkina et al). Unfortunately, the methods of determining the afore-mentioned biochemical changes in rickets are very complicated, are feasible only in well-equipped biochemical laboratories and cannot therefore be recommended for general practice.

The diagnostic value of determining the activity of alkaline phosphatase is questionable. However, most authors mention increased phosphatase activity in normally nourished children during the development of the rachitic process. The increase does not always correspond to the severity and period of the disease. Diminished phosphatase is more constant in rickets developing against the background of hypotrophy.

Roentgenography often fails to confirm the diagnosis of rickets in its early phase. Clear changes in roentgenograms are characteristic of far advanced cases; they very well reflect the dynamics of the process and the course of healing during treatment.

Only a deep analysis of clinical symptoms exhibited by the child can decide the diagnosis in early rickets. Anamnestic data are also of definite value. The physician examining the child for the first time must find out all about the family's living conditions, as well as the child's regimen and character of feeding.

No diagnosis of rickets should be made on the basis of one or a few signs. Good knowledge of the symptoms of this disease during the various phases of its development is necessary. Changes in the osseous system, irregular and late dentition, late closure of the fontanel, muscular

hypotonia and retarded static and motor development may also be observed in other diseases, and this must always be borne in mind.

Ossification defects of the cranial bones discovered at the time of birth are sometimes ascribed to congenital rickets. To begin with, this phenomenon is found in children born underweight and in prematurely born children in whom the processes of bone development have not reached the state they do in full-term, well-developed children. The localisation of the softened parts of cranial bones at the time of birth also differs from that in rickets. Congenital ossification defects are usually found in the temporal bones, one or both. They are arranged as a narrow band along the sagittal or lambdoid sutures and involve considerable portions of the temporal bones. Depending on their intensity these softenings disappear by the end of the first or the beginning of the second month of life. Roentgenograms of the limbs show no deviations from the normal structure; the calcium and phosphorus content is also normal.

Rachitic softenings of bones appear in the second or third, but most frequently between the fourth and sixth month of life and are localised along the edges of the bones, imperceptibly merging with the unaffected tissue.

It should be remembered, however, that rickets may also develop in infants 4-8 weeks old. This is usually observed in prematurely born children and those who had some sort of disease in the first month of life. The rachitic process begins, as in infants 3-6 months old, with excessive sweating (mainly of the head) and restlessness. This is followed by alopecia occipitalis, pallor of the skin, muscular atonia and, within 1.5-3 weeks, craniotabes. In such early rickets it is sometimes possible to observe roentgenographically typical bony changes: moderate osteoporosis, thinning and erosion of the preparatory calcification zone, and indistinct contours of the distal metaphysis of the forearm bones, mainly the radius. In most cases the

blood serum shows diminished phosphorus (from 4.3 to 2.7mg%) and sometimes calcium. Thus, groundless restlessness, excessive sweating and a pale skin even in infants 1-1.5 months old must attract the attention of physicians and suggest possible rickets (Z. G. Korolyova).

Osteoporosis arising for various reasons and causing various skeletal deformities may also lead to an erroneous diagnosis of rickets. Severe dystrophic cases resulting from malnutrition, caused by protein, vitamin and mineral salt deficiency give rise to peculiar *osteopathias* (M. F. Maretskaya and M. D. Kurbatova). But in these cases the epiphyses are not thickened, there is no hypophosphatemia, and the calcium is considerably diminished. Roentgenograms clearly show osteoporosis, but there are no changes in the epi- and metaphyseal parts of the bones pathognomonic of rickets. Anti-rachitic treatment is either of little avail or completely ineffective, and only adequate nutrition with a lot of vitamins and mineral salts leads to improvement and subsequent recovery.

Retarded dentition, late closure of the fontanel, arrested motor development, retarded growth and an enlarged abdomen are always observed in infants with *hypothyroidism*. All these symptoms may serve as the basis for diagnosing rickets, but more careful observation permits of making a correct diagnosis.

In the child affected with hypothyroidism the skin is dry, rough and appears thickened ("mucous edema"), especially on the neck. Such children are considerably retarded in their mental development. No softening of the cranial bones is ever observed in these cases; the edges of the anterior fontanel do not close for a long time, but they are hard. The epiphyses are not thickened and there are no rosaries. Roentgenograms show no characteristic changes except greatly retarded appearance of the ossification nuclei.

Chondrodystrophy or achondroplasia is a congenital disease in which the contours of the child's body are sim-

ilar to those of a rachitic from the very moment of birth. In this disease the growth of bones in length is disturbed, the bones of the limbs appear thickened and a difficulty of movement in the joints is observed. The skin and subcutaneous tissue develop normally. This leads to formation of transverse folds, especially on the legs. Such children have very short arms and legs. In an upright position the freely hanging arms barely reach to the navel, whereas in normally developed children they come down to the middle of the thighs. Since the main phalanges of the three middle fingers are shortened, the hands of such patients look like tridents, while the fingers are of equal length. The skull is enlarged and has sharply developed frontal and parietal eminences, the nose is saddle-shaped, and brachycephaly is in evidence. The neck is short, lordosis is strongly pronounced, the abdomen is large and protruding. The skin is flabby, no excessive sweating is observed, and there is moderate muscular hypotonia.

Roentgenograms show very characteristic changes in the bones, but they are unlike the changes occurring in rickets. The bones appear shortened and compact and have a marked periosteal band, sometimes transverse bands (pathological calcification zones) arranged parallel to the epiphyseal ossification line. In the growth zone the cartilage cells are arranged irregularly, instead of in the form of even columns; the junctions between cartilage and bone are affected.

In some children the chondrodystrophic phenomena are not so clearly marked or are manifested only in disturbed growth of the bones of the upper or lower limbs.

Congenital bone fragility is characterised by multiple fractures which lead to various skeletal deformities. However, the fractures differ from those occurring in rickets. They are not greenstick fractures but complete fractures with displacement of the fragments. They are usually multiple and can be observed in all the bones of the skeleton. They occur both in and *extra utero*, imperceptibly and

without any apparent reason. Numerous calluses form at the sites of the fractures and cause severe skeletal deformities. Not infrequently the skull of children with fragile bones is unusually soft and pliant. The bones are thin and atrophic, the muscles are flabby, the ligaments and joint capsules are stretched and relaxed. The children are very backward in their physical development, are highly excitable and are sometimes noted for their precocity. The scleras have a characteristic bluish tinge.

Roentgenoscopy shows porosity of the bones, slurred outlines, a thinned cortical layer, shortened tubular bones and vaguely outlined calluses. The boundary between the epiphysis and diaphysis is distinct and thin. Unlike rickets, there are no changes in the epi- and metaphyseal zone.

Mongolian idiocy with all its characteristic symptoms can hardly be mistaken for rickets. However, in the beginning the clinical picture is not very clear, and it is therefore necessary to differentiate the symptoms of these two diseases. Skeletal deformities, especially those of the thorax, muscular hypotonia, late and irregular dentition, late fontanel closure, increased excursions of the joints and arrested motor development observed in Mongolian idiocy may also be exhibited in severe forms of rickets, but there are many characteristic signs which facilitate a correct diagnosis.

In the first place these children have a brachycephalic skull with a sloping occiput, a flat nose, squinting eyes with the inner angles of the eyelids lowered and narrow palpebral fissures. Exophthalmos, strabismus and nystagmus may be observed. The children always keep their mouths open with the tongue frequently sticking out and characteristic abundant salivation. The skin is cold, marbleised and intensely pigmented, as though rouged, on the cheeks and chin. The ears are of irregular shape. Children affected with this disease lag in mental development, do not know their close relatives, are inclined to grimacing and repeating the same movements, learn words with dif-

ficulty and do not understand their meaning. In mild cases some children acquire certain practical skills and elementary knowledge. The prognosis is unfavourable. The etiology of the disease is unclear. Pathoanatomical examinations reveal changes in the cells of the nervous tissue and the endocrine glands.

Young, inexperienced physicians may mistake *congenital dislocation of the hip* for rickets, since in such cases children begin to walk late and waddle as in cases of rachitic curvature of the femoral neck. The limbs seem shortened because of the high position of the trochanters. Roentgen pictures of the pelvic bones make things clear.

It is difficult to confuse rachitic kyphosis with *spondylitis*, if it is remembered that the latter develops in older children than do rachitic curvatures in whose formation not one or two, but many more, vertebrae take part, for which reason in rickets the spine curves in the form of a flat arch and does not produce an acute angle. With the child in a prone position the rachitic curvature straightens out, especially if the child's legs are raised. This does not take place in tuberculous spondylitis. In doubtful cases a careful clinical examination and a roentgen picture may make things clear.

Severe *scurvy* in infants exhibits symptoms similar to those of rickets.

In scurvy the child has painful bones and muscles due to hemorrhages; it is restless when touched, is unwilling to move and has thickened epiphyses of the long bones of the limbs and pathological changes in the ribs resembling a rosary. But in such cases the ribs are often displaced with respect to the cartilages and together form broken, zigzag lines. Changes in the skin and mucous membranes in the form of punctate or more extensive hemorrhages typical of vitamin C deficiency can be found or easily produced. Young erythrocytes are found in the urinary sediment.

Roentgen data also differ from those in cases of rickets by showing a "fragment zone", considerable osteoporosis and slurred outlines of the bones. In severe forms of scurvy in children roentgenograms show subperiosteal hemorrhages.

Anamnestic data on the child's regimen prior to the disease and blood tests for vitamin C help to make a correct diagnosis.

Congenital syphilis is now a rare occurrence, but since such possibilities are not completely excluded this disease must also be considered. The disease may be confused with rickets because of the periosteal stratifications on the cranial bones and the epiphyses of the long bones, the bowlegs and enlarged liver and spleen; in these cases bosselated cranial eminences appear earlier and are more strongly pronounced than in rickets. The curvatures of the shank bones are periosteal stratifications rather than real curvatures. The child affected with congenital syphilis has a characteristic appearance. The peculiar tinge of the skin (waxy-yellowish), the nose persistently secreting mucus which causes infiltration of the surrounding tissues, the scars around the mouth and anus, the enlargement of all groups of lymph nodes and, in some cases, the skin eruptions point to a correct diagnosis. The serological reactions in young children are usually negative, and the blood of the parents has to be analysed. The changes in the bones shown in roentgenograms are particularly distinct and permit of a correct diagnosis even in the absence of the typical skin disorders; the preparatory calcification zones are enlarged and marked osteochondritis is evident; these symptoms are not characteristic of the rachitic process.

PREVENTION

Measures for prevention of rickets must be initiated before the birth of the child. In this respect health education plays an important role; it consists of lectures and talks on the causes of rickets and measures to prevent it. The pregnant woman must be impressed with the great importance of an optimum regimen for her own health and for the proper development of the fetus. An adequate diet with a lot of vitamins, and plenty of sunshine may lead to an accumulation in the woman's organism of vitamins A, D, C and group B, as well as mineral salts, necessary to prevent rickets in the child.

Expectant mothers are advised to take for the same purpose one or two courses of ultraviolet irradiation of 15-20 sessions each, especially in the autumn and winter, during the last two months of pregnancy. It has been found that irradiation of pregnant women with a quartz lamp diminishes the possibility of rickets developing in children (K. A. Krutikova).

According to many authors, saturation of the pregnant woman with vitamin D prevents development of rickets in the offspring because it creates a vitamin D depot in the organisms of both mother and fetus. However, nobody has as yet convincingly demonstrated the existence of such a depot, and administration of vitamin D even in massive doses only during pregnancy fails to produce desirable results.

Liebe added calciferol to the food of pregnant women for a period of 3 months before childbirth, and in subsequent observations over a period of 3-6 months discovered rickets in 35 per cent of their children. At the same time he found clear manifestations of rickets at the age of 3-6 months in a greater number (52.4 per cent) of children whose mothers had not been given vitamin D during pregnancy.

For the purpose of preventing rickets pregnant women were given condensed milk containing equal amounts of vitamins D_2 and D_3 for a period of 4-5 months before childbirth. The total daily amount of the preparation contained 1,600 u of vitamin D, and yet 29 per cent of the children born of these mothers were found to have rickets during the first 3 months of life. Later studies failed to confirm the possibility, mentioned in literature, of preventing rickets only by consumption of massive doses of vitamin D during pregnancy. It was demonstrated experimentally (B. S. Ginsburg) that the liver of the fetus does not form a substantial vitamin D depot. This has made it clear that women have to be given vitamin D not only during pregnancy, but also during the period of nursing. Some authors prescribe a weekly dose of 200,000 u of vitamin D_2 for a period of 2 months before and 2 months after childbirth (A. I. Titova, Y. I. Grachova, V. M. Tretyakova, M. P. Mechkovskaya), others—from 200,000 to 300,000 u twice a month or from 700,000 to 900,000 u a month for a long period of time (5-6 months) and produce a considerable effect.

It is not advisable to administer single massive doses of vitamin D because systematic saturation does not require such large doses.

The observations conducted by B. K. Mikis have shown that prolonged consumption of the vitamin (for 3 months before and 3 months after childbirth) in small doses (1,500 u) does not safeguard all children against rickets, although it does produce some favourable results. First degree rickets was found in 13 per cent of the children

whose mothers had been given vitamin D and second degree rickets in 2 per cent of the cases, whereas in children whose mothers had not received vitamin D milder forms of the disease were found in 41 per cent and moderately severe forms in 6 per cent of the cases.

Considerable success in preventing rickets can be achieved by giving women 5,000-10,000 u of vitamin D_2 daily during the last two months of pregnancy and for 3-4 months of nursing. Whenever possible nursing mothers should receive 1 tablespoonful of cod-liver oil (vitamins A and D_3) 2 or 3 times a day. It is very necessary to give them 1,000 mg of ascorbic acid and 5 mg of vitamin B_1 every day. All vitamins pass in large measure from the mother (through the placenta and the milk) to the child and thus help to prevent rickets (M. N. Bessonova, M. I. Andreyeva, L. A. Lebedeva et al).

Saturation of the nursing woman's organism with vitamins D, C, etc., is necessary because under the usual dietary conditions human milk contains very little vitamin D (about 4 u per 100 ml—A. T. Petrayeva, Y. F. Dombrovskaya) and up to 4 mg of vitamin C in summer and about 2.5-2.9 mg% (average) in autumn and winter. Within 25-30 days systematic daily consumption of 100 mg of ascorbic acid raises its level in the human milk from 2.5-2.9 to 4-5 mg%, increases the amount of fat and alters the correlations of the protein fractions in the milk by increasing the noncasein fraction (V. A. Bogdanova).

It has been established that administration of vitamins A, D, C and group B to expectant and nursing mothers produces a more favourable effect than administration of calciferol alone. No manifestations of rickets in the children born of such mothers were observed over a period of 6-8 months (P. D. Davydov).

Post-natal prophylaxis requires primarily a good external environment for the proper development of the child. It is extremely important to keep the child outdoors as long as possible all through the year. Not even the most

thoroughgoing airing of the child's room can make up for it. The child must be taken outdoors from the age of 10-12 days during the warm time of the year and 3-4 weeks after birth in autumn and winter. During the summer months the child must be kept in the shade the greater part of the day.

The child may be exposed to the sun for prophylactic purposes. To produce an anti-rachitic effect, it is enough to expose separate parts of the body—arms, legs, face. Even if the child wears a short shirt and panama hat and is kept in the shade (under an awning) but out in the open, it will benefit from the reflected rays of the sun. In early childhood exposure to the sun must be limited and employed with extreme caution. Indiscriminate exposure to the rays of the sun may lead to overheating the child, burns and other harmful consequences. Children may be given a course of sun baths (15-20), preferably under observation of medical personnel (in children's institutions), providing caution is exercised and their reactions are watched. Exposure to the sun must begin with 1-2 minutes and be brought up to 20-30 minutes, depending on the climatic conditions, especially the intensity of insolation. Total exposure to the sun must begin only at 1.5-2 years of age.

It is also very good to keep the child outdoors in winter for, although insolation is less intense, the fresh, cold air enhances the oxidative processes in the organism and helps to harden the upper respiratory tract. Out in the open the child soon falls fast asleep, the outdoors creating better conditions for protective inhibition.

But since the time the child is kept outdoors in winter is limited and the insolation is insufficient the child does not get enough ultraviolet rays and must therefore be given a course of sun lamp radiations. The exposure to these radiations aimed at preventing rickets should begin at the age of 1-1.5 months, especially of children predisposed to rickets (prematurely born, twins, frequently ailing infants and those fed artificially or kept on a mixed diet).

The irradiation sessions may be conducted only when a

requisite temperature (not below 20°C) is maintained in the room, making sure that the sunlight lamp is already turned on. Irradiations must begin with $^1/_8$-$^1/_4$ biodose and must be gradually increased to 1.5-2 biodoses. A course of irradiations consists of 15-20 sessions (Y. D. Zabludovskaya) and must be repeated every 1.5-2 months, depending on the character of feeding, the nutritional status and general regimen of the child.

The child's development is favourably influenced by physical exercise and the child must therefore be given every chance to move about freely both at home and in children's institutions. When awake, the child must be unwrapped and left for several minutes, at first half-undressed and then completely naked. Such air baths, in addition to hardening the organism, are necessary for the child's motor development. All nurseries and children's homes must have facilities for laying out infants, and various devices and apparatus to crawl about and climb. To prevent rickets, children must be systematically given massage and exercise. These methods favourably affect the nervous and muscular systems and the internal organs (respiratory and circulatory), and enhance metabolism. The physicians and community nurses of health centres and polyclinics must teach the mothers how to bring these necessary physical influences to bear on the child's organism.

Breast-feeding is one of the most important prophylactic measures. Although breast-feeding does not completely prevent rickets, it is generally known that breast-fed children have this disease less frequently and, what is even more important, never have its severe forms. With the mother's milk the child receives all the nutrient substances which fully cover the child's needs up to 5-6 months of age. The mineral substances (phosphorus and calcium) and enzymes contained in human milk ensure their better assimilation by the child's organism. Breast-fed children are less frequently affected with gastrointestinal diseases, while gastrointestinal dysfunction which, as is well known,

affects assimilation of phosphorus and calcium, may lead to a deficiency of these substances in the child's organism and thus facilitate the development of rickets. From 5-6 months of age children must be given additional food containing minerals and vitamins. In cases of mixed and artificial feeding this must be done sooner. Vegetable and fruit (especially citrus) juices may be given to children at the age of 1.5-2 months, beginning with 2-3 drops and gradually increasing the amount. The best additional food is grated vegetables, raw berries and fruit, and cereals cooked with vegetable or beef broth. Too many farinaceous foods—cereals, cakes, buns, noodles, milk jellies, etc.—must be avoided. Excessive carbohydrates in the food disturb the synthesis of vitamins A, D, C and B, and are conducive to development of rickets.

Not all phosphorus and calcium compounds in the food are well assimilated by the organism. Inositolhexaphosphoric acid found in large amounts in cereals, especially in oatmeal and in maize and maize flour, disturbs calcium absorption and precipitates calcium in the intestines, excluding it from further participation in metabolism (Hövels, Albright). In cases of insufficient consumption of vitamin D with the food or its inadequate formation in the organism and predominant content in the food ration of the aforesaid carbohydrate substances calcium salts may be washed out of the bones (V. N. Smotrov). From the age of 3-4 months it is good to add to the food a boiled egg yolk, at first every other day and then daily. It is also good to give 5-6 months-old children grated fish liver or roe by adding 1-2 teaspoonfuls of them to the grated vegetables or cereal 2-3 times a week. These substances do not produce great anti-rachitic effect, but they are highly nourishing (full value proteins, easily assimilable fats, mineral substances), which necessitates their addition to the infant's ration.

To improve the diet of young children and facilitate the work of mothers, packing plants in the U.S.S.R. are now

producing vegetable, fruit and berry juices, vegetable, fruit and berry purées, vegetable and beef-and-vegetable soups, dry vegetable and flour mixtures and various milk and flour mixtures. They are prepared of high-quality raw material, under strict sanitary conditions and laboratory control and are recommended even for infants under 1 year of age. The nutrient value and customary taste of the products from which these canned foods are made are preserved. These foods are readily assimilated because they are very finely ground. The vitamins are also much better preserved in them.

Fruit purées are produced in the following assortment: apricot purée, apple purée, apple purée with rice, apple purée with milk and prune purée. These products may be given to healthy infants as early as the fifth or sixth month of life, as additions to cereals. Moreover, apple purée and apple purée with rice are dietetic products which children consume with great benefit in cases of colitis. Prune purée may be given to children past 8 months of age with habitual constipation. Canned vegetables—split pea soup with milk, squash purée with milk, spinach purée with milk and carrot purée are very palatable and nourishing foods containing considerable amounts of mineral salts (potassium, phosphorus, calcium) and vitamins A, B_1, B_2, P, PP and C. These foods should be recommended for children from the age of 7 months and, in cases of artificial or mixed feeding, sooner. Carrot purée may be given to healthy children from the age of 6 months. In cases of gastrointestinal dysfunction carrot and squash purées diluted with rice water produce a good therapeutic effect because they are rich in pectins, carotene, and calcium, phosphorus and iron salts.

This beef-and-vegetable soups are very palatable and convenient; they can be given to children as additional food as soon as the children have learned to eat vegetable and fruit purées. Thick liver soup is particularly recommended and it may be given to artificially fed children to prevent

rickets sooner (from the age of 6 months) than to breast-fed children (from the age of 8 months).

However, no prophylactic measures are complete without additional administration of vitamin D. From the end of the very first month of life children must be given 2,000-3,000 u of vitamin D_2 with human milk daily all year round, except the summer months, if they spend the greater part of the day outdoors. Under unfavourable climatic and unhygienic conditions, as well as in cases of prematurely born, artificialy fed, malnourished and frequently ailing children the dose of vitamin D_2 must be increased to 4,000-5,000 u and must be given uninterruptedly. Fish liver oil is a very effective prophylactic. It can be given to infants from 1-1.5 months of age in doses of 2-3 drops, from 2 months—half a teaspoonful and from 3 months—a teaspoonful 2 or 3 times a day. Fish liver oil is readily assimilated by most children; if the gastrointestinal tract functions normally it may also be given in the summer (it must be bought in small portions and kept in a cool place). Fish liver oil is superior to calciferol, a vitamin D_2 preparation, because it also contains vitamin A which is likewise indispensable for the growing organism. Not all children take fish liver oil willingly because of its unpleasant taste; in some children it causes gastrointestinal dysfunction. Moreover, there is no assurance that by taking fish liver oil the child receives the necessary amount of vitamin D, because in most cases its anti-rachitic activity is unknown.

Administration of massive doses of vitamin D_2 once in 1-3 months for prophylactic purposes, recommended by some physicians, may be resorted to only if there is no assurance that the mother will systematically give the child fish liver oil or vitamin D_2 every day or if the child lives very far from a medical institution.

It has been established by many recent studies that administration of vitamin D_2 or D_3 does not always prevent rickets. Jung and Sanchez found symptoms of rickets in 60 per cent of the children systematically given vigantol for

prophylactic purposes. Administering vitamin D_3 parenterally in a dose of 6,250 u and in a more massive dose of 25,000 u to prematurely born children Niedner found manifestations of rickets from the age of 3-4 months in two-thirds of the children under observation. In cases of artificial or mixed feeding the rachitic process develops at an earlier age (1-1.5 months) (Eck, Gabrielsen and Halvorsen).

Hence, even timely and prolonged administration of vitamin D does not always safeguard children against rickets. This serves as incontestable proof that rickets is not only a vitamin D deficiency disease, and it is therefore necessary to give children plenty of the other vitamins. In many cases systematic consumption of fruit and vegetable juices fails to meet the requirements in these vitamins, especially in prematurely born, artificially-fed and frequently ailing children, as well as in cases of failure to observe the rules of hygiene. It is therefore necessary daily to administer for prophylactic purposes (in addition to vitamin D) 30-35 mg of ascorbic acid and 3 mg of thiamine all through the autumn, winter and early spring without interruption.

Prophylaxis of rickets must continue ceaselessly for 2-3 years, i.e., as long as the child may contract the disease. In the Soviet Union infant health centres, polyclinics, nurseries and children's homes take all necessary measures to prevent rickets in the children under their supervision. Systematically watching the health and development of the children and maintaining close contact with their mothers, the physicians and nurses are in a position to improve the health education of the population by carrying their knowledge to each family. They talk to the people individually and in groups, lecture, speak over the radio and contribute to the local press. This purpose is also served by seasonal exhibitions and wall newspapers. The struggle for proper breast-feeding, good care and observance of the rules of hygiene is a struggle for a healthy child. A big part is played by the "motherhood schools" which cater to

masses of women. Conferences of mothers with physicians reporting on the health of the children of the district and on all measures carried out for the purpose of preventing rickets, hypotrophy, infectious, gastrointestinal and other diseases are a very interesting form of health education. There are many organisational forms of health education and the infant health centres have extensive experience in this respect.

All debilitated, prematurely born, artificially-fed and frequently ailing children, as well as twins, must be kept under constant medical observation and must be provided for by special rickets prevention programme. To discover early symptoms of rickets (before involvement of the bones) and be able immediately to institute treatment physicians must examine children under 2 years of age every month. Children's institutions must keep records not only of the children with moderately severe and severe forms of rickets, but also of those with mild forms. The accounts of children's medical institutions must reflect the total rickets incidence (all forms). Measures aimed at preventing rickets must be carried out permanently rather than at some particular period.

Massive doses of vitamin D_2 for prophylactic purposes must not be administered indiscriminately because in some cases this is likely to prove harmful, especially to children with nutritional disorders. Since vitamin D is not an agent that completely ensures prevention of rickets, it is necessary to carry out the entire complex of measures which enhance the reactivity of the child's organism. In addition to proper natural feeding and general hygienic regimen, small doses of vitamin D given together with vitamins A, B and C may prove very effective. Mercury vapour lamps (source of long-wave ultraviolet radiation) may be used in nurseries and children's homes for daily systematic irradiation in autumn and winter. According to D. M. Dyomina's observations (1957), daily irradiation with one-eighth ultraviolet radiation dose produces a complete enough anti-

rachitic effect without affecting either the hemopoietic function or the increase in weight

Sanitary measures must be carried out more extensively in summertime. Infant health centres and polyclinics can greatly contribute to children's health by organising summer playgrounds and promenade groups so that the children of working mothers can spend the greater part of the day outdoors, take sun and air baths, and receive adequate, freshly prepared food. Moving the nurseries and children's homes to the country for the summer months every year is a tried and tested health-building method.

Proper organisation of the child's surroundings, especially in children's institutions, is indispensable for rickets prevention and reduction of general child morbidity.

TREATMENT

Phosphorus had long been used in the treatment of rachitic children, its use being based on the experiments of Wegner who, having produced rachitic changes in the bones of animals kept on a phosphorus and calcium deficient diet, subsequently observed sclerosis of bones in the same animals administered small doses of phosphorus (quoted from Y. M. Lepsky).

In 1887 A. A. Kisel concluded on the basis of his experimental studies that administration of phosphorus in rickets produced no therapeutic effect. In his dissertation he stated that no one had been able to prove the benefit of phosphorus in rickets and since its use was fraught with danger he thought it best to relinquish it.

I. A. Shabad held that of the phosphorus and fish liver oil mixture it was not the phosphorus but the fish liver oil that helped in rickets. Until the 1920's the latter was considered the most reliable remedy.

Many believed that the active principle in the therapeutic activity of fish liver oil was vitamin A and that rickets was caused by a deficiency of this vitamin. It was subsequently demonstrated, however, that fish liver oil continued to be effective even after destruction of vitamin A in it. Soon another vitamin with marked anti-rachitic activity was isolated from the nonsaponifying part of the fat and was given the designation of vitamin D.

The main source of vitamin D is the oil obtained from the liver of fish. The oil of many species of fish contains much more vitamin D than does the widely used cod-liver oil; this applies to the oil obtained from halibut, bullhead, sea bass and tuna. The anti-rachitic activity of the liver oil of the Murmansk cod is lower (10-40 u per 1 ml) than that of the Baltic cod (80-250 u per 1 ml). Fish liver oil is not only a vehicle of vitamins A and D, but is also the most assimilable of all animal fats. According to some observations, addition of fish liver oil raises the percentage of assimilation of the fat contained in all the food.

Pediatricians have made many attempts to find a more effective oil (animal, fish) for the treatment of rickets. The therapeutic action of sea bass liver oil was tested for this purpose by M. M. Levit and E. S. Mikhlina. Prolonged administration of this oil—for 2-3 months—slightly improves the phosphorus and calcium balance and the bone calcification process. Diminished sweating and irritability are observed clinically. In some cases the pliancy of the cranial bones diminishes.

Dolphin liver oil proved still less effective. Slightly diminished hypophosphatemia and a negligible improvement in the calcification process were found after 2 months' administration of this oil; in some children it improved sleep and decreased the sweating.

The widely used cod-liver oil is also insufficiently effective in the treatment of moderately severe and severe forms of rickets. No appreciable improvement in the process is noted after 12-14 weeks of its administration to children (S. Y. Shaferstein et al).

But despite the aforesaid, fish liver oil must be prescribed not only for prophylactic purposes, but also as a therapeutic agent. Fish liver oil contains vitamin D_3 identical in structure to the vitamin found in the human organism. Vitamin D_3 is more effective (50-100 per cent) than vitamin D_2. Moreover, fish liver oil contains vitamin A which is indispensable for the growing organism. But in treating chil-

dren with marked rickets it is necessary, in addition to fish liver oil, to administer concentrated vitamin D_2 or D_3 preparations, since it is in this way possible, when necessary, to administer a large amount of vitamin in a small volume of preparation.

A mercury vapour lamp—source of ultraviolet radiation—has come to be used since the 1920's. Huldschinsky published a study reporting that he had succeded in completely curing rickets by means of ultraviolet rays. The softenings of the occipital bone, the bracelets on the upper and lower limbs and the rosary had disappeared in the course of irradiation (4-6 weeks). In a number of cases dentition had been observed and the static functions had considerably improved. Appearance of the reparative process had been discovered roentgenographically. Biochemical changes had also been noted; the level of phosphorus in the blood had risen and acidosis had diminished.

This method of treating rickets had also won the approval of many Russian pediatricians. After 20-30 sessions of ultraviolet irradiation the rachitic symptoms disappear in about the following order: irritability and sluggishness are replaced by activity and liveliness, sweating ceases, sleep and appetite improve, craniotabes, softening of the fontanel edges, thickening of the epiphyses and other pathological manifestations in the osseous system diminish. The calcium and phosphorus level in the blood rises. The motor skills improve within 1.5-2 months of the beginning of the treatment (B. I. Badanov, F. M. Rotstein).

Simultaneously with the discovery of the anti-rachitic action of ultraviolet rays it was found that certain foodstuffs (vegetable oil, milk, spinach) which do not possess anti-rachitic properties acquired them when exposed to the action of ultraviolet rays; because of the sterols (ergosterol, cholesterol) contained in the foodstuffs a number of substances were formed, including active anti-rachitic substances of the vitamin D group (György, Popoviciu, Bills, Tolnai, Hess). Ergosterol found mainly in vegetable

products forms a vitamin designated as vitamin D_2, while cholesterol found in animal products and tissues forms vitamin D_3.

Since this discovery was made irradiated preparations of cholesterol, ergosterol and various foodstuffs have been widely used in the treatment of rickets. Irradiated milk has been very extensively prescribed to rachitic children. It has been established that not only liquid milk but also milk powder acquires an anti-rachitic property when exposed to ultraviolet radiation. Addition of irradiated yeast or ergosterol to the ration of cows enriches the milk with vitamin D (György, Ienke, Lewis, MacLeod).

Some authors ascribed the positive effect of the milk powder enriched with vitamin D in the treatment of rachitic children not only to the presence of the vitamin, but also to the large amount of calcium contained in cow's milk. Although this method of treatment produced favourable changes in the condition of rachitic children, it was nevertheless impossible to administer with irradiated milk powder the requisite amount of vitamin D in a short period of time. That is why rickets could not be cured even within 8-12 weeks. Besides, feeding children milk powder produces a deficiency of vitamins, especially C and group B.

The vitamin D_2 preparation now used for prevention and treatment of rickets is ultraviolet-irradiated ergosterol. Vitamin D_2 (calciferol) is industrially manufactured in the Soviet Union by the Trufanov method (irradiation of concentrated benzol solutions of ergosterol derived from yeasts).

Vitamin D_2 is a high molecular solid alcohol. It is a colourless, odourless and tasteless crystalline substance, soluble in fats, ether and alcohol, with a melting point of 115-117°C. Heated to 115°C without admission of air vitamin D_2 does not lose its biological activity, while heating to 125°C destroys calciferol and inactivates the vitamin. Vitamin D_2 is also unstable in the light. Dissolved in vege-

table oil and stored in air-tight vessels in the dark it retains its activity for a number of years.

First derived in its chemically pure form from fish liver oil in 1936-37 vitamin D_3 is relatively resistant to oxidation and can withstand high temperatures; boiling does not diminish its content in foodstuffs. Vitamin D_3 is much less toxic than vitamin D_2 and possesses greater anti-rachitic activity.

Vitamin D is the only (known) vitamin present in ordinary food in very small amounts. More of it is found in animal fats (fish liver oil, summer butter); it is also contained in the roe and liver of fish, and in lesser amounts in egg yolks and milk (summer).

In the child's organism vitamin D_3 forms under the influence of ultraviolet rays from the provitamin (7-dehydrocholesterol) found in the blood of the skin capillaries. It forms particularly actively in very young children whose skin is rich in sterols. A sufficiency of vitamin D in the child's organism depends on several factors, the most important of which are constant prolonged irradiation of the child with ultraviolet rays of a definite wavelength, consumption of this vitamin with the food, and an appropriate diet containing enough full-value proteins, fats, carbohydrates, mineral salts and vitamins in correct proportions. Utilisation of vitamin D in the organism largely depends on the proper functioning of the liver and normal digestion. Digestive disorders disturb the assimilation of vitamin D consumed with the food, hamper absorption of phosphorus and calcium salts, increase their loss through the intestinal tract and pervert the processes of intermediate metabolism.

In 1934 an international commission of vitamin experts adopted a 0.01 per cent olive oil solution of irradiated ergosterol as a standard for vitamin D and 1 mg of this standard as the unit of vitamin D activity. This corresponds to 0.025 μg of vitamin D (1 μg = 0.001 mg).

At first a 1 per cent vegetable oil solution of irradiated

ergosterol was used for the treatment of rickets. According to many physicians, this preparation was much more effective than fish liver oil. Vitaminol containing 2,000 u of vitamin D_2 per 1 ml was synthesised in 1934. This has made it possible to dose vitamin D more accurately. But it was administered in small doses—20,000-30,000 u per course of treatment—which only slightly improved the rachitic process, 30-40 days of treatment failing to cure the patients. Better results were observed after the doses had been increased to 120,000 u for a course of treatment (4,000 units daily for a period of 1 month), but physicians were still dissatisfied.

In 1938-40 it was reported that rachitic children could be cured with a single massive dose (600,000 u) of vitamin D. According to these reports this method of treatment increased the phosphorus and calcium in the blood within 48 hours and clinical signs of improvement were observed within 5 days. Normal roentgen pictures were obtained within 7-13 days. No manifestations of hypervitaminosis were noted (Harnapp, Vollmer, Brockmann).

According to many authors, a single massive dose of vitamin D produces a therapeutic effect apparently because the vitamin is deposited in the organism. Assumptions have been voiced that many organs—the liver, kidneys, adrenals, thymus, muscles, skin and fatty tissue—can serve as depots. But it is still unknown precisely in what organs vitamin D administered in large doses is deposited. Numerous experimental studies have failed to answer this question.

The method of shock therapy of rachitic children has attracted the attention of pediatricians by its simplicity, accessibility, rapidity of action and considerable effectiveness. In the U.S.S.R. this method began to be used in 1938. This opportunity presented itself as soon as the Moscow Vitamin Manufacturing Plant started producing a highly concentrated vitamin D_2 preparation (100,000-150,000 u per 1 ml). In the beginning no more than 400,000-450,000 u

was prescribed for a course of treatment. The entire dose was administered in 3-6 days. The therapeutic effect of this treatment was appreciable, but not so striking as had been noted by the foreign authors. According to E. S. Moshkevich, roentgenograms of the distal ends of the forearm showed changes in the form of beginning calcification only 18 days after administration of large doses of vitamin D_2 and of marked ossification within 35-45 days.

According to the author's observations, treatment of rachitic children with large doses of vitamin D_2 (100,000 u a day for 6-7 days) first improves the patients' neuropsychic state. About 10-12 days after the beginning of treatment the depression, sluggishness, inactivity and apathy are replaced by cheerfulness, buoyancy and activity; the children begin to sleep better and it is easier to make contact with them; they greet adults with a smile, readily laugh and take an interest in toys. Perspiration diminishes or completely disappears.

Changes in the osseous system are the second clear sign of improvement in the rachitic process after treatment with vitamin D_2. The cranial bones harden (in cases of craniotabes, softening along the cranial sutures and edges of the anterior fontanel) within 2-3 weeks of the beginning of treatment, and in children with nutritional disorders—later (within 1.5-2 months). Dentition (in cases of delayed dentition before the treatment) is observed within 12-14 days, and in severe forms of rickets—within a month.

The deformities of the osseous system resulting from excessive growth of osteoid tissue—bosselated parietal eminences, rosary, bracelets—persist unchanged for a long time. The reason for it is that the osteophytes which have formed calcify and their complete elimination is possible only in cases of feebly marked rickets. Very stable also are the changes produced by the process of osteomalacia—cranial deformities (sloping skull, olympian forehead, etc.), thoracic deformities (expansion of the lower aperture,

pigeon breast, transverse constriction) and curvatures of the lower limbs.

Muscular hypotonia and abnormal joint mobility persist for a rather long time after treatment with vitamin D_2. A slight improvement in the muscle tone of normally nourished children with moderately severe forms of rickets is observed within a month, whereas in rickets involving dystrophy signs of improvement can be observed only within 2-3 months and even later.

In normally nourished or slightly underweight children improvement of the static and motor functions is noted within a month. Towards the end of the second month the motor skills correspond to age. Children with second or third degree rickets or extremely undernourished children lag in the development of their motor functions much more. Positive changes in this respect are noted within 2-3 months only in cases of improved nutrition.

In 40-50 per cent of the children normal appetite and normal stool appear by the end of the second or third week. Considerable improvement in the children's nutrition is therefore observed only within 1.5-2 months. After stable improvement in the rachitic process the children begin to gain weight, but the gain is not uniform and depends on the severity of the disease, the state of nutrition and the child's age. In severe forms of rickets, especially those involving dystrophy, the weight gain in the course of the month is insignificant; normally nourished children or those with first degree hypotrophy gain more weight.

Hence, the effectiveness of treatment with vitamin D_2 varies not only with the severity of the process, but also with the child's nutrition; treatment with massive, as well as usual, doses of vitamin D proves less effective in cases of chronic nutritional disorders.

Administration of large doses of vitamin D_2 (100,000 u for a period of 6 days) raises the blood phosphorus and calcium level towards the end of the first week. In these

cases phosphorus increases 1.5-2 mg%, calcium—much less, i.e., 0.5-1 mg%; the mineral metabolism indices are normalised within 3-4 weeks. In children treated with usual doses (50,000 u for a period of 2 weeks) the phosphorus content in the blood increases less appreciably, i.e., about 0.8-1 mg%, and within 28-30 days reaches 4.5-4.8 mg%. In some cases the amount of calcium slightly decreases in the second or third week (0.8-1.2 mg%), but soon becomes normal again.

The therapeutic effectiveness of vitamin D_2 is manifested in an improvement of the balance of the other vitamins and of the enzymogenic function.

One month after treatment the level of vitamin C in the blood rises from 0.29-0.34 to 0.57-0.68 mg% without additional administration of this vitamin. Vitamin B_1 metabolism also improves, but less significantly. The activity of the serum alkaline phosphatase increases if it was diminished before treatment; if the activity of the enzyme was increased before treatment, it diminishes within 1-2 months to normal (M. N. Bessonova).

Under the influence of vitamin D_2 treatment the roentgenograms of most children show the beginning of the reparative process, but the intensity of the process varies with individual cases. One month after treatment the roentgenograms of 90 per cent of normally nourished children even with moderately severe forms of rickets show the preparatory calcification zone to be more compact, the cortical layer distinct, and the ossification nuclei enlarged; in 80 per cent of the children osteoporosis diminishes or disappears. In cases of rickets involving second and third degree hypotrophy signs of marked reparation are observed 1.5-2 months after treatment. Normalisation of the bony structure in normally nourished children is found within 8-10 weeks, and in cases of marked nutritional disorders—towards the end of the third or fourth month. The restorative process is particularly slow in hypotrophic children affected with intercurrent diseases.

Recovery from rickets can often be ascertained roentgenographically only within 4-5 months.

The time of appearance of the first reparative changes and the subsequent course of the reparative process largely depend not only on the child's nutritional status, but also on the severity of rickets and its phase in the beginning of the treatment; in convalescent children treatment with massive doses of vitamin D is an impetus that hastens recovery.

Vitamin D is not effective in all cases of rickets. The reason for it is that in rickets there is a deficiency not only of vitamin D, but also of other vitamins, especially ascorbic acid and thiamine. Combined administration of vitamins produces a greater therapeutic effect. Ascorbic acid is best administered per os in small doses of 100 mg. Massive doses of ascorbic acid are not assimilated by the organism of the affected child, the greater part of it being destroyed in the organism and a lot of it excreted in the urine. Excretion of large amounts of organic acid cannot but affect the kidneys. It is therefore more rational to administer vitamin C in small doses for a long time, until complete healing. To compensate for vitamin B_1 deficiency, the latter must be administered in doses of 4-5 mg, depending on age.

The author's experience shows that administration of vitamins C and B_1 simultaneously with vitamin D produces a greater therapeutic effect manifested in an improvement of the osseous system. One month after treatment with vitamin D_2 (600,000 u) 15-20 per cent of the children showed no perceptible clinical improvement in the bone symptoms of rickets, whereas in cases treated simultaneously with vitamins D_2, C and B_1 absence of improvement was noted only when the patients were affected with intercurrent diseases during the treatment of rickets. In cases of combined vitamin treatment the process of dentition improves, from 2 to 5 teeth erupting (in individual children) one month after saturation with ascorbic acid and

vitamins B_1 and D_2, and from 4 to 8 teeth—within two months. Vitamins C and B_1 intensify the process of osteogenesis by influencing the formation of the normal histological structure of bones (vitamin C), the oxidative and reductive processes and mineral metabolism, and by stimulating the phosphatase—the enzyme participating in phosphorus metabolism.

Vitamins C and B_1 diminish muscular hypotonia and, consequently, contribute to developing the static and motor functions of rachitic children. Signs of muscular hypotonia are observed in 45-50 per cent of the children treated only with vitamin D_2 as late as two or three months after treatment even when given systematic massage and exercise. In children with marked nutritional disorders myopathy disappears only within 6-8 months, after improvement in their nutritional status. Only 10-14 per cent of the children (suffering from hypotrophy and gastrointestinal diseases) administered thiamine and ascorbic acid fail to show appreciable improvement by the end of the second month.

The author is inclined to ascribe the very good effect produced on muscle tone by the combined administration of vitamins to the fact that a rise in the level of ascorbic acid and vitamin B_1 in the organism improves phosphorus metabolism, which is indispensable to normal metabolism in muscle tissue. Moreover, it diminishes the disintegration of muscle protein with formation of creatinine, which is observed in cases of vitamin C deficiency (A. V. Palladin), and improves the processes of assimilation. Formation of glycogen in the liver and muscle tissue also improves. Administration of ascorbic acid enhances adrenal function, which is very important, for it is well known that vitamin C deficiency leads to development of hypotonia as a result of the diminished hormonal function of this organ. However, the increased trophic influence of the central nervous system is particularly important.

The improvement in the functional state of the nervous system and the increased muscle tone are conducive to a more rapid development of the child's static and motor functions. After elimination of vitamins C and B_1 deficiency the pains in the bones and muscles caused by the minute hemorrhages under the periosteum and into the muscles, which occur in severe forms of rickets with marked avitaminosis, cease (Y. F. Dombrovskaya, Y. M. Lepsky, A. T. Petrayeva, M. N. Bessonova).

The effect of vitamins C and B_1 administered in combination with vitamin D_2 is particularly evident in the improvement of the functional state of the gastrointestinal tract and, consequently, in enhancing the children's nutrition. The children's appetite noticeably improves and the motor functions of the intestines are normalised. As a result of saturation with ascorbic acid and systematic administration of thiamine the stool is normalised in the overwhelming majority of children by the end of the second week. In cases treated only with massive doses of vitamin D an unstable stool persists for a long time in 40-45 per cent of the children (suffering from intestinal dysfunction before the treatment).

Simultaneous administration of vitamins D_2, C and B_1 improves metabolism and enhances the processes of assimilation. Children of the first year of life gain 600-650 g in one month after the beginning of the treatment.

The better results of combined administration of vitamins are due to the stimulatory influence of ascorbic acid and vitamin B_1 on the secretion of the gastrointestinal glands. Secretion of gastric juice improves. The acidity and pepsin content increase. The functions of the liver and pancreas become normal; more trypsin, lipase and amylase is produced by the pancreas and more esterase by the liver (S. M. Ryss, T. N. Yermakov). The normalisation of the intestinal functions in a considerable number of children after administration of vitamins C and B_1 can be explained by elimination of the deficiency in these vitamins,

since diarrhea and sometimes a spruelike stool are often observed in cases of hypovitaminosis (B. A. Lavrov, A. V. Leonov).

The hemopoiesis in children treated with massive doses of vitamin D_2 improves but slightly. The amount of hemoglobin remains unchanged or increases 2-3 per cent; the number of erythrocytes does not change, although in some cases it increased by 200,000-300,000; the colour index is unaffected; the phenomena of anisopoikilocytosis persist. No noticeable changes in the leukocytes can be discovered; in cases of considerable leukocytosis before the treatment, the shift of the leukocytic formula to the left remains and the leukocyte count somewhat diminishes but does not reach the norm.

Considerable improvements in the blood occur in children treated simultaneously with vitamin D_2, C and B_1. Within 3-4 weeks the amount of hemoglobin increases 7-9 per cent (average), the erythrocyte count increases from 3,000,000-3,750,000 to 4,000,000-4,250,000, the colour index rises from 0.6-0.7 to 0.8-0.84, and normalisation of the leukocytes is observed, i.e., anisocytosis and poikilocytosis are noted in single cases, and anisochromia is absent (M. N. Bessonova).

The mineral metabolism indices are also normalised much sooner. Simultaneous administration of vitamin D_2, ascorbic acid and thiamine causes a rise in the phosphorus level in the blood to 4.5 mg% and calcium to 9.7 mg% during the very first week after the beginning of the treatment; by the end of the second week the amount of phosphorus is 4.8-5 mg% and calcium—10-10.5 mg%. Owing to this, roentgenograms show the beginning of calcification in the meta- and epiphyseal parts of the long bones within one week. The signs of osteoporosis disappear particularly rapidly.

Various studies published in recent years assert a higher effectiveness of the treatment of rachitic children with massive doses of vitamin D_2 in an alcohol solution. They, furthermore, maintain that vitamin D_2 in alcohol eliminates

mainly the symptoms of the nervous and osseous systems and improves the oxidative processes (E. A. Raikher, Y. N. Davydova, N. P. Bulygina, N. V. Chernakova, T. I. Garsevanishvili).

The author made extensive use of highly concentrated vitamin D_2 preparations in oil and alcohol solutions, but was unable to find any particular difference in the antirachitic activity of the two preparations. However, if it is necessary to administer massive doses in the treatment of young children showing signs of dystrophy and gastrointestinal disorders, it is best to prescribe vitamin D_2 in an alcohol solution because this preparation does not affect the digestive functions and is more willingly taken by children. If the usual method of treatment is employed, vitamin D_2 in a weaker concentration is recommended; this is particularly convenient in treating children at home.

It follows that the effectiveness of the treatment is determined not only by the dose of vitamin D and the quality of the preparation, but also by the child's nutritional status, the severity of the rachitic process and the sum total of the other measures which enhance the activity of the vitamin preparations. Subsequently the child's health depends on his surroundings. Failure to observe the rules of sanitation and hygiene, improper feeding and lack of fresh air may again lower the calcium and phosphorus level in the blood and bring about a relapse of the rachitic process within a month's time.

Intercurrent diseases (influenza, measles, whooping-cough, pneumonia, gastrointestinal and other affections) hamper the therapeutic activity of vitamins D, C and B_1 in rickets, and may bring about a relapse of the disease. In such cases it is necessary to repeat the course of antirachitic treatment. It is indispensable if the child contracts tuberculosis or a protracted form of dysentery. The treatment of such children must be complex, prolonged and repeated two or three times. All diseases disturb metabolism, especially the oxidative and reductive processes, thus

aggravating the acidosis present in rickets and necessitating prolonged administration of vitamins C and B_1. Moreover, if the organism is saturated with vitamins, all acute and chronic diseases run a more favourable course. In treating prematurely born rachitic children the vitamins must be administered for a longer period and the treatment must be repeated in autumn and winter.

It should be remembered that it is impossible to eliminate hypovitaminosis only by administration of a particular vitamin. Vitamin deficiency may be caused by a number of endogenous factors. Endogenous hypovitaminosis develops either as a result of poor absorption of the administered vitamin from the intestines (in digestive disorders) or because of its insufficient utilisation by the organism. The latter may take place in acidosis which develops as a result of frequent attacks of infectious diseases and disorders of the hepatic functions.

The role of the liver in the emergence of endogenous hypovitaminosis is connected with the difference in the action of vitamins D_2 and D_3 in the organism. According to a number of authors, vitamin D_2 is active only when administered per os, while its parenteral administration diminishes its therapeutic effect. Vitamin D_3 forming in the skin by irradiation of children with ultraviolet rays or by irradiation of dehydrocholesterol of animal fats is active and effective when administered both per os and parenterally. From this the conclusion is drawn that administered per os vitamin D_2 at first undergoes certain changes, apparently in the liver, after which it becomes active. This may explain why vitamin D_2 treatment of extremely undernourished children with hepatic dysfunction is ineffective (S. O. Dulitsky, Heymann).

Rickets may be difficult to cure in prematurely born children also because of endogenous hypovitaminosis and that is why such children must not be administered large doses of vitamin D_2. The lowered reactivity of the child's organism in cases of dystrophy, protein and mineral de-

ficiency, avitaminosis, and deep-rooted disorders of the functions of the liver, pancreas and other organs diminish the assimilation of vitamin D_2, as well as of the other vitamins. In such cases positive changes after the treatment are determined, as was already mentioned, not so much by the severity of the rachitic process as by the state of the child's nutrition. *Administration of massive doses of vitamin D_2 to extremely undernourished children may lead to still greater depression of the hepatic functions, cause deeper disorders of metabolism and aggravate the rachitic process.*

A negative reaction to large doses of vitamin D_2 may be particularly frequently observed in prematurely born children with chronic nutritional disorders during the first year of life. The reaction is manifested in loss of appetite, gastrointestinal dysfunction (vomiting, diarrhea), general depression, sluggishness and loss of weight. It is manifested with still greater force, if the child is not administered vitamins A, C and group B. Administration of these vitamins counteracts the negative effect of large doses of vitamin D by its favourable influence on the metabolic processes and digestive functions.

Vitamin D preparations may give rise to phenomena of hypervitaminosis. Toxic doses are many times as large as the usual doses administered for the treatment of rickets. Administration of large amounts of vitamin D, i.e., the so-called shock method of treatment, or its prolonged administration for therapeutic or prophylactic purposes even in usual doses may cause hypervitaminosis.

Feeble symptoms of hypervitaminosis are observed quite often, but they are not always diagnosed. In such cases there may be nausea, at times vomiting, inappetence, failure to gain weight and gradual dystrophy.

The literature of recent years contains reports of severe manifestations of hypervitaminosis—vitamin D superfluity—in children long administered different doses of concentrated alcohol or oil vitamin D_2 preparations.

Ross and William observed four cases of vitamin D_2 intoxication, in which infants (from 8 to 14 months of age) were given biosterol in doses of 20,000-40,000 u for a period of several months. Each child received a total of 2,820,000-4,800,000 u of vitamin D_2. Two children (twins 10 months old) died. Autopsy revealed degenerative changes and deposits of calcium salts in the myocardium, alveolar walls, muscle, basal and epithelial cells of the stomach walls and in the epithelium of the renal tubules and glomeruli.

In 1949 Debré and Brissaud reported 85 cases of severe vitamin D intoxication observed by them personally and described by other authors.

V. A. Vlasov and V. K. Stolyarova observed (1957) 10 children 4-12 months old with severe symptoms of hypervitaminosis admitted to the clinic with toxic dyspepsia or toxicoses of unclear etiology. All these children had received various doses of vitamin D_2 in an alcohol solution (200,000 u per 1 ml) over a period of 1-4 months. The highest total dose administered to any one child was 13,500,000 u, the lowest—6,000,000 u.

According to all authors, the symptoms of intoxication develop gradually and their severity does not always correspond to the amount of vitamin consumed. Severe cases show extreme underweight and appreciable changes in the central nervous system—apathy or excitement, sleepiness or insomnia, clonic or clonicotonic spasms. The skin becomes greyish-yellowish, lighter on the flexor surfaces, dry, and peels. Loss of appetite sometimes develops to the point of total anorexia, thirst increases and nausea, vomiting (up to 10-15 times a day at the height of the intoxication) and intestinal disorders (constipation or frequent stool) appear. Examination of the gastric juice reveals achylia. The liver and, in some cases, the spleen are enlarged. Extension of cardiac dullness, dull sounds, inconstant systolic murmur and tachycardia are observed. The arterial pressure is elevated. Electrocardiograms show

deep changes in the ventricular muscle and slow conduction. Urinalysis shows albumin in the urine, 20-50 leukocytes and 2-3 erythrocytes in the field of vision, single casts and an increase in calcium salts.

Marked calcemia (14.5-22.8 mg%) is found in all cases of vitamin D intoxication; the amount of phosphorus is normal or somewhat below normal.

Roentgenograms of bones show an expanded zone of preparatory calcification in the epiphyses of the shank and forearm bones in all children and a thickened cortical layer in some.

Examination of the eyes sometimes reveals calcium deposits in the cornea and on the conjunctiva (E. S. Mikhlina, V. A. Vlasov and V. K. Stolyarova, Debré and Brissaud).

The child's organism is greatly harmed not only by the severe hypervitaminosis, but also by the more frequently observed mild intoxication. Pediatricians must therefore prescribe vitamin D preparations without exceeding the recommended doses and the duration of their administration. If it is necessary to treat a case by the "shock" method, it should be done only in a hospital or polyclinic. Vitamin A in a dose of 2-3 mg must be simultaneously administered in all cases. Administration of vitamin B_1 (in the same dose) is also very important for, according to A. T. Zhmeiko and S. N. Matsko's experimental data, *administration of vitamin B group preparations inhibits the development of hypervitaminosis* even when toxic doses of vitamin D_2 are added to the fodder of animals.

Vitamin D_2 in highly concentrated solutions of either alcohol or oil (200,000 u per 1 ml) must not be prescribed for home treatment or prophylaxis. It is best to use an oil solution containing no more than 50,000 u of vitamin D per 1 ml. Simultaneous administration of fish liver oil is beneficial only in cases of administration of small doses of the vitamin for therapeutic purposes. *Rachitic children*

must not be irradiated by mercury vapour lamps at the period of administration of vitamin D_2.

To prevent rickets, it is best to use fish liver oil containing vitamins. When prescribing vitamin D to children, physicians must inform the mother of the harm of its excessive administration, and of the dose and duration of its administration in each individual case.

During the treatment, especially with large doses, it is recommended (E. S. Mikhlina) that the urine should be tested for calcium every 5-6 days by the Sulkovich method. For this test 3-4 ml of urine is mixed with an equal amount of Sulkovich's reagent (2.5 ml of ammonium oxalate, 2.5 ml of oxalic acid, 5 ml of strong acetic acid and 140 ml of distilled water), the degree of turbidity offering a tentative idea of the amount of calcium in the blood.

Slight turbidity (+) corresponds to normal calcium content in the blood, i.e., 9-10 mg%. Clearly marked turbidity (+ +) appears in the urine when the blood contains 11-13 mg% calcium; intense turbidity (+ + +), as though by addition of milk, denotes a calcium level of more than 13 mg% in the blood, i.e., considerable hypercalcemia.

In cases of hypervitaminosis it is necessary, first of all, to discontinue administration of vitamin D, and administer 3-4 mg of vitamin A, 4-5 mg of thiamine and 300 mg of ascorbic acid a day until all intoxication symptoms disappear. Administration of large amounts of liquid (physiologic saline and Ringer's solutions) orally, subcutaneously and intramuscularly, hypertonic (20 per cent) glucose solution intravenously, and a 25 per cent magnesium sulfate solution intramuscularly in doses of 0.2 per 1 kg of the child's weight relieves the child's condition. Cardiacs are administered according to indications. Repeated administration of 50-60 ml of plasma (intravenously) and, after elimination of toxicosis, transfusion of 30-40 ml of blood produce a good therapeutic effect.

The treatment of rachitic children requires an individual approach as regards the dose of vitamin D and the

method of its administration. The severity and period of the disease, the child's age and nutritional status, intercurrent diseases, living conditions, character of feeding, care and all other circumstances must be taken into account.

In the initial period of first degree rickets breast-fed infants must be given 8,000-10,000 u of vitamin D_2 in human milk every day (in 2 doses) for a period of 1-1.5 months. Subsequently, depending on the course of the reparative process, they must be administered 4,000-5,000 u a day all through the autumn and winter. For undernourished children and those with an unstable stool it is advisable to prescribe an alcohol solution of 15,000-20,000 u of vitamin D_2 a day for 2-3 months and then 5,000-6,000 u a day during the autumn and winter.

At the height of moderately severe rickets (second degree) the dose of vitamin D_2 must be increased to 25,000-30,000 u a day to be administered likewise in milk in two doses for a period of 1-1.5 months. If necessary, the treatment must be repeated within 1.5-2 months. During the intervals between the courses of treatment administration of the preparation must be continued in a daily dose of 5,000-6,000 u.

Children with third degree rickets must be given vitamin D_2 in a daily dose of 50,000 u for 12-14 days or 100,000 u for 6-7 days. The treatment may be repeated 2-3 times with intervals of 1-2 months depending on the clinical, roentgenographic and biochemical data, as well as the environmental conditions. During the intervals between the courses of treatment vitamin D_2 is administered in a dose of 6,000-8,000 u, depending on the child's nutritional status, character of feeding, care and gastrointestinal functions.

In order to prevent a relapse all children of the first 3 years of life who have survived rickets must take vitamin preparations in doses of 5,000-8,000 u a day during the autumn and winter.

The anti-rachitic value of fish liver oil has already been dealt with. It will be remembered that its administration is as necessary for therapeutic as it is for prophylactic purposes.

Administration of fish liver oil is recommended simultaneously with a vitamin D_2 preparation. Administration of the oil must begin with several drops, the dose gradually increasing to a teaspoonful. Up to the age of 6 months infants must be given 1 teaspoonful twice a day, from 6 to 12 months—two or three times a day, and children 1.5-2 years of age—1 dessertspoonful twice a day.

Although the method of treating rickets with vitamin D is completely justified and in most children results in restoration of phosphorus and calcium metabolism, and improvement in the neuropsychic status and symptoms of rachitic bone lesions, there are also cases in which treatment with vitamin D alone fails to produce the desired result and does not eliminate the rachitic myopathy, anemia and a number of bone symptoms of rickets; the static and motor functions are not always restored. In day-to-day practice there are also cases in which administration of vitamin D preparations fails to produce any improvement even in the osseous system, which has engendered the idea of so-called vitamin-D-resistant forms of rickets (Albright, Butler, Bloomberg). This confirms that the pathogenesis of rickets is very complicated and that it requires complex therapy. The treatment must be aimed at restoring normal metabolism, trophics and functions of the organs and systems of the organism. Measures of general influence on the organism, control of acidosis, disturbances of oxidative processes, demineralisation, anemia, vitamin deficiency and other phenomena must play an important part in the treatment of rachitic children, especially if they are affected with dystrophy.

Ascorbic acid and thiamine must be administered in the treatment of all forms of rickets. Children at the height of second and third degree rickets must be given at least

100 mg of vitamin C and 3-5 mg of vitamin B_1 for a long time, i.e., until clearly marked reparation is observed. In cases of chronic nutritional disorders, especially with concomitant diarrhea, it is best, if possible, to administer the vitamins parenterally. In cases of intercurrent infectious diseases, for example, pneumonia, the dose of ascorbic acid must be increased to 300-400 mg and that of thiamine to 10 mg.

In addition to vitamin D_2 preparations, ascorbic acid and fish liver oil, it is also necessary to prescribe calcium. Administration of calcium is particularly beneficial during the period of convalescence when mineral metabolism improves, absorption of calcium in the intestines and deposition of calcium salts in the bones increase, and the child's organism needs greater amounts of mineral substances. Calcium may be administered with fish liver oil or in the form of a 10 per cent calcium chloride solution, and powdered calcium lactate and calcium gluconate. Some authors recommend simultaneous administration of phosphorus preparations in the form of phytin and calcium glycerophosphate (M. S. Maslov, Y. M. Lepsky, Z. B. Doroshevich, et al).

Reports on the good effect of *videine*, a new preparation (combination of vitamin D_2 with proteins and the products of their hydrolysis) have appeared in the press (A. M. Khvul, V. P. Bendt). It has been established that within 4-5 days of the beginning of the treatment, in addition to the improvement in the child's general condition (normalisation of sleep and increase in appetite), the level of inorganic phosphorus and, later, calcium in the blood rises and calcification of the bones improves. In clinical tests this preparation was administered in very large doses—600,000-800,000 u for 3-6 days in first degree rickets, 800,000-1,200,000 u in second degree rickets, and 1,200,000-1,600,000 u in third degree rickets. All the children given the anti-rachitic treatment were hospitalised in connection with pneumonia and other diseases.

Although insufficient knowledge has as yet been gained concerning the effectiveness of administering vitamin D_2 in combination with protein preparations, the available data already indicate that administration of protein in the treatment of rachitic children is of certain benefit. It has been experimentally demonstrated that diminished protein (9 per cent instead of 18) in the food ration of growing animals (white rats) leads to morphological changes in the bones of the extremities resembling the changes obserbed in rickets. The therapeutic effect of vitamin D depends on the protein content in the food ration (M. I. Olevsky).

Rickets is characterised by disorders of the hepatic functions, including the protein function (Y. M. Lukyanova), which aggravates metabolic disorders and hinders the reparatory processes in the treatment of children with vitamin D.

Diminished reabsorption of amino acids in the renal tubules and their excessive excretion at the height of rickets are also conducive to disorders of protein metabolism. The excessive excretion of amino acids in the urine continues for a long time and becomes normal only on complete recovery from rickets. Aminoaciduria is particularly high in children with so-called stubborn forms of rickets which are not amenable to treatment with vitamin D (Fishman, Jonxis, Royer, Spahr, Gerbeaux).

It has been reported that severe forms of rickets, resistant to vitamin D, are cured by oral administration of cow's blood serum diluted with rice or barley water with an addition of pancreatine. According to the reports, neither mercury vapour lamps nor vigantol were used in the foregoing therapy (Reinlein, Geering).

The aforesaid authors explain the effectiveness of this method by the fact that the serum proteins, mainly of the globulin type, with a low content of calcium and phosphorus in the medium of high caloric carbohydrates lead to normalisation of the metabolic processes disturbed in

rickets. Moreover, administration of animal blood serum leads to an increase in the globulin fraction of the children's blood, which may account for their greater resistance to infections observed when this method of treatment is used.

That is why administration of plasma or normal human serum in complex treatment of rickets may prove still more effective, especially in cases of severe forms of rickets involving chronic nutritional disorders. Administration of plasma and serum is recommended in the usual age doses (8-5 ml per 1 kg of body weight) 3-4 times at 4-5-day intervals, depending on the severity of the rachitic process and the child's nutritional status. Stimulatory treatment is also effective for children between 1.5 and 3 years of age; the treatment consists of a course of 6-7 intramuscular injections of 3-5 to 10 ml of their parents' blood at 2-3-day intervals. Particularly good results are observed in children with marked anemia, when anti-anemin (cobalt-containing liver extract), compalon and other liver preparations are simultaneously administered.

Since the glycogenic function of the liver is disturbed in severe forms of rickets accompanied by considerable muscular hypotonia, it is necessary to administer glucose without fail together with vitamins C, B and PP.

To eliminate acidosis which, along with other factors, hampers ossification of the bones and leads to extreme metabolic disorders, it is recommended to administer, together with vitamin D, 5-6 g of citric acid or 2-3 g of sodium citrate. This helps to maintain the acid reaction in the intestines, facilitates absorption of calcium and phosphorus in the intestines and diminishes acidosis (Y. M. Lepsky, M. B. Kokhanova). Fruit and vegetable juices containing a large amount of mineral substances have the same mechanism of action. But to produce a positive effect, the child must be given at least 50-100 ml of juice a day, which, in many cases, may cause gastrointestinal dysfunction and for which reason administration of the juice

must begin with small doses, the latter being gradually increased to the requisite amount.

As yet there is no complete agreement concerning the effectiveness of sodium citrate or citric acid. Some authors believe that calcium forms compounds with citric acid in the intestines and this retains the calcium in the organism. As soon as enough calcium ions accumulate in the zones of bone growth, calcium and phosphorus salts are deposited there. According to Heinz, Müller and Rominger, citric acid is necessary for the prevention and treatment of rickets and in the future it will be administered as an anti-rachitic agent along with vitamin D, since it is a chemically simpler substance. Other authors hold that sodium citrate and citric acid are either ineffective in rickets (Carlgren) or even diminish calcium and phosphorus assimilation, affecting the balance of these mineral substances (Cramer, Porrata-Doria, Steenbock).

Corbisterol acetate and 7-dehydrocholesterol acetate exposed to ultraviolet rays acquire anti-rachitic properties and in experiments on rats have exhibited equal therapeutic activity (Rosenberg).

Soviet pediatricians have always paid particular attention to diet in rickets; this question has now been elaborated in detail. In feeding rachitic children it is necessary to take their inclination to acidosis into consideration. The amount of farinaceous food which contains phosphorus in a form poorly assimilated by children must be limited. A diet abounding in farinaceous foods leads to an unfavourable $\frac{Ca}{P}$. Children's food must contain fewer acid and more basic valences. Milk, bread, cereals, flour and fats contain an excess of acid valences, while vegetables and fruits contain more basic valences. Vegetables, especially foliar, contain a lot of calcium, which is important for rickets characterised by disordered mineral metabolism.

The maximal shift of the acid-base balance in the direction of acidosis is observed at the height of the disease

and during convalescence. An excess of fats must be avoided because they affect the absorption from the intestines of the calcium consumed with the food; in such cases a large amount of fatty acids binding the calcium are formed and the calcium is then excreted from the organism as salts of fatty acids. The binding of calcium by fatty acids in the intestinal lumen also affects the assimilation of phosphorus from the food.

The child's food must contain sufficient full-value proteins which are particularly necessary as plastic material forming part of every cell in the organism. Enough proteins in the food ensure assimilation of calcium and phosphorus, which is extremely important for the child's normal development, as well as for prevention and treatment of rickets.

Consumption of enough full-value proteins with the food is indispensable if the vitamins are fully to perform their functions. A deficiency of full-value proteins in the food may hinder the assimilation of vitamins by the organism. The reason for this is that "proteisation" of the vitamins —binding by specific proteins—is necessary for their function. It was convincingly demonstrated by Academician A. V. Palladin in his report on the "Physiological Role of Proteins in the Diet" to the Third All-Union Conference on Vitamins (Moscow, December 12-18, 1944). These close functional connections between vitamins and proteins may also determine the influence of vitamins on assimilation and utilisation of proteins by the organism.

Normal metabolism can be ensured only by a definite correlation between the protein component of the food and the vitamin B complex, ascorbic acid and vitamins A and D it contains. Diminution of protein in the food reduces the ability of the organism to deposit vitamins B_1 and B_2 and nicotinic acid. At the same time more of these vitamins is excreted with the urine. Protein deficiency weakens vitamin A synthesis. Subsequent inclusion in the diet of pro-

teins, corresponding to physiological requirement, brings everything back to normal (A. V. Trufanov).

In the chapter dealing with prevention of rickets the author already discussed the questions of feeding. It is therefore unnecessary to re-enumerate the foods to be given to the rachitic child and the forms in which they are to be consumed. It will do well, however, to recall the particular importance of fruit and vegetable purées, meat and vegetable soups, canned minced liver, egg yolks and fish roe, which must constitute a considerable part of the rachitic child's diet.

Physical Methods of Treatment. In complex treatment of rickets, in addition to a proper hygienic regimen, an adequate diet with enough irradiated (enriched with vitamin D_3) fish liver oil or preparations of vitamins D_2, C and group B, as well as stimulatory agents, extensive use must also be made of the available methods of physiotherapy. Ultraviolet irradiation is still one of the most effective physiotherapeutic methods.

Ultraviolet rays produce various effects on the organism of the rachitic child; administration of vitamin D does not fully replace ultraviolet irradiation.

Observations of children living in northern regions, where the climatic conditions do not permit of natural ultraviolet irradiation of the open parts of the body even in summertime, have shown that an adequate diet with enough fats and vitamins, including vitamin D, does not safeguard them against rickets to the extent that does systematic exposure to a weak source of ultraviolet rays 2-3 hours a day for 2 months even without additional administration of vitamin D (D. M. Dyomina, A. P. Zabaluyeva, I. S. Kandror).

Ultraviolet rays exert an influence directly on the central nervous system. Changes leading to formation of vitamin D_3 occur in the skin exposed to them. Moreover, irradiation is attended with coagulation of protein and damage to the protoplasm of the cells, resulting in formation of products of protein decomposition some of which possess

high biologic activity (histamine, acetylcholine, etc.). These substances stimulate the cells and tissues locally, and through the circulatory, lymphatic and nervous systems stimulate a number of organs and systems of the human organism (gastrointestinal tract, liver, kidneys, etc.) (Y. D. Zabludovskaya).

It has now been demonstrated that, in addition to its own metabolism, the skin actively participates in the biological processes of the organism as a whole. That is why its exposure to ultraviolet rays enhances not only mineral metabolism, as has been demonstrated by many researchers (P. S. Medovikov, F. M. Rotstein, B. I. Badanov), but also all the other forms of metabolism.

Ultraviolet irradiation produces a number of changes in the functions of various organs and systems of the organism (gastrointestinal tract, the cardiovascular and respiratory systems). Small doses of ultraviolet irradiation considerably improve the digestive processes. In cases of moderate rachitic anemia the red elements of the blood regenerate much faster under the influence of ultraviolet rays (young forms appear in the blood and the amount of hemoglobin increases). The leukocyte picture shows at first slight neutrophilia and subsequently lymphocytosis and eosinophilia. It should be remembered, however, that ultraviolet rays, especially of a shorter wavelength, possess hemolytic activity, and immoderate doses of the rays may cause considerable diminution of the blood hemoglobin (Y. D. Zabludovskaya). Mercury vapour lamp treatment must therefore be conducted under control of clinical blood tests.

Ultraviolet rays produce a particularly important effect on the immunobiological reactions of the child's organism. It has been found that they may cause an increase in the titer of the specific antibodies, agglutinins, precipitins, etc., and stimulate the phagocitic ability and enzymatic activity, thus altering the reactivity of the organism.

Until recently it was held that simultaneous ultraviolet

irradiation and administration of vitamin D_2 was inexpedient and even harmful since it could produce hypervitaminosis. Observations have shown, however, that administration of fish liver oil, medium doses of vitamin D and systematic irradiation of the child lead to quicker and stable recovery rickets. If it is necessary to administer massive doses of vitamin D in a short period of time, the vitamin treatment must be administered first and the patient exposed to ultraviolet radiation afterwards. This method must be employed systematically in the treatment of all rachitic children until complete recovery.

Ultraviolet irradiation is contraindicated for children with pulmonary tuberculosis, nephritis, extreme emaciation, marked anemia and cardiac decompensation.

Experimental studies and clinical observations show that ultraviolet irradiation stimulates increased assimilation of phosphorus and calcium consumed with the food, fish liver oil and vitamin D preparations and eliminates various disorders caused by vitamin C deficiency. It is therefore very expedient to give the child, all through the course of irradiation, food rich in mineral substances and vitamins, and, additionally, calcium and phosphorus preparations, ascorbic acid and thiamine.

The patients must be exposed to general radiations, beginning with 1/6, 1/4, 1/3 and 1/2 erythema dose. To determine the necessary dose, not only the child's age, but also the severity and period of the disease and the child's general condition are taken into account. For example, during the initial period of first degree rickets it is recommended to begin irradiation with 1/4 erythema dose on alternate days, a course of treatment consisting of 20 sessions. For infants 3-6 months of age and undernourished children under 1 year of age it is best to begin the first 2-3 irradiation sessions with 1/6 erythema dose for the anterior and as much for the posterior surface of the body and gradually increase the irradiation to $2^1/_4$-3 erythema doses for each side of the body. Each session must last not

more than 15-20 minutes to avoid tiring the child and producing a negative reaction. At the height of second and third degree rickets, especially if the disease runs an acute course, the irradiation should begin with 1/4, 1/3 and less frequently with 1/2 erythema dose (25 sessions for the course of treatment). During the periods of convalescence and residual phenomena, as well as in protracted and relapsing forms of rickets the treatment must begin with 1/4 erythema dose and consist of 25 sessions (Y. D. Zabludovskaya).

If the child has unfavourable living conditions, is improperly fed, does not get enough fresh air and does not receive vitamins D, C and group B it must be given larger doses of irradiation.

In cases of first degree rickets and favourable external environment one course of irradiation is enough. In all other forms of the disease it is necessary to repeat the courses of treatment with intervals of 1.5-2 months.

In severe, advanced forms of the disease the patients must also be exposed to ultraviolet radiations in summertime, the climatic conditions permitting, especially in large industrial cities.

Ultraviolet irradiation produces a favourable effect only when combined with a rational diet and proper general regimen. Fresh air plays an extremely important part. Systematic walks and sleep out in the open in the daytime even in autumn and winter greatly contribute to both prevention and treatment of rickets. In winter it is particularly beneficial to the child to stay outdoors on sunny days between 11:00 A.M. and 2:00 P.M. when solar radiation is especially intense. In winter a favourable effect is also produced by reflection of the sun's rays. The walks and sleep outdoors are beneficial only if the child's face is uncovered as long as the child is outdoors.

Outdoor sleep in winter is superior to sleep on a glazed veranda because the glass completely excludes the most active rays of the solar spectrum, i.e., the ultraviolet rays,

and the organism actually finds itself in "biological darkness" (Y. Y. Ginsburg, D. V. Messel).

The sun's rays (their ultraviolet part) are a valuable agent for preventing and treating rickets. S. F. Khotovitsky wrote the following about the curative effect of the sun in rickets, as far back as 1847 (in *Pediatrics*): "A salutary effect is produced by a so-called air, or more so, sun bath, when the young child wearing only a shirt is placed in a sandbox and is allowed to spend the day out in the open, moving about and frolicking in the sun".

It should be remembered, however, that exposure to the sun's rays requires the same caution as irradiation by a mercury vapour lamp. No sun baths are recommended for infants under 1 year of age, for whom they are replaced by light and air baths in the shade near a sunlit place. In cases of light and air baths the child's organism is simultaneously influenced by light and air, which is also very important for hardening the organism. Sun and air baths taken properly and systematically train the thermoregulating apparatus, stimulate the nervous system and improve the blood circulation, metabolism and other functions. The methods of using sun and air baths were described in the chapter on prevention of rickets.

Rubdowns, affusions, showers and baths are a valuable aid in the treatment of rickets. The baths most frequently used are: brine, brine and conifer extract, and conifer extract baths; sponging with water containing salt or cologne, affusions or showers are also very helpful.

Brine baths enhance the metabolism of rachitic children (V. V. Kufayev) and intensify the oxidative processes, greatly improve the children's general condition, appetite and sleep, and diminish their irritability and excitability.

Baths with water containing 1 per cent sodium chloride produce a more lasting and intense hyperemia of the skin than do fresh water baths. Baths containing 3 per cent sodium chloride increase the excretion of urine and chlorine ions, and diminish the excretion of nitrogen. Baths with

a still higher concentration (6 per cent) of sodium chloride inhibit excretion of liquid, and increase the excretion of nitrogen, calcium and phosphorus (Grüninger).

Brine baths are indicated for normally nourished children and, especially, for those slightly overweight because they may lead to a slight loss of weight. These baths are not recommended for emaciated and very excitable children because of possible sleep disturbances and loss of appetite and weight. Some positive effect is produced in these cases by baths containing conifer extract.

Baths produce a good effect after ultraviolet irradiation on children past 6-8 months of age at the height of the rachitic process or during the convalescent period; they must be taken for 10-15 minutes 2-3 times a week, with the water at 35-36°C; the course of treatment must consist of 10-12 baths, depending on the child's reaction. Subsequently the temperature of the water may be gradually lowered to 32°C, but the room temperature must not be below 19°C. Brine or conifer extract baths should be followed by affusions with colder (1-2°C) clean water. The child's body must be dried and lightly rubbed down if the skin is not sufficiently hyperemic. After the bath the child must be put to bed.

Affusions and showers are very healthful for children from 1.5-2 years of age in the summer following sun baths, the affusions and showers lasting 30-60 seconds with the water temperature not below 30-32°C.

Baths and showers are not specific anti-rachitic agents, but used systematically they favourably affect the child's nervous system, stimulate it and thus enhance its regulatory influence on all the metabolic processes and functions of the organs and systems of the body, which is manifested in considerable improvement of the child's general condition and normalisation of sleep and appetite.

Sand baths are well tolerated even by very young children. Sand is hygroscopic and slightly heat-conducting; heated by the sun's rays it gives children a pleasant sensa-

tion of warmth. It is advisable to give children sun baths on the seashore or a river bank. The combination of the fresh, pure and moist air with sunshine and heat benefit the child's organism.

Many authors have demonstrated that diathermy is productive of a good therapeutic effect in rachitic myopathy. The arms and legs of children with muscular hypotonia are usually cyanotic and cold to touch. The thermal effect of diathermy—deep heating of the limbs—is of considerable therapeutic value.

Heat improves the blood and lymph circulation, eliminates venous stasis, enhances tissue metabolism and improves the nutrition of muscle fibres. Diathermy is also of no little value as an analgesic. Diminution of pain may contribute to motor improvement.

To produce a lasting therapeutic effect, it is necessary to conduct 20-30 diathermy sessions of 10-25 minutes each. According to Y. D. Zabludovskaya's observations, the muscles become more elastic and the children's movements more active after only 5-6 sessions. Towards the end of the treatment children begin to walk, if they are supposed to according to their age. In third degree rickets, especially in cases combined with dystrophy, treatment with diathermy must be conducted for a longer period. The effect of the treatment is enhanced when it is accompanied by massage, physical exercise, ultraviolet irradiation and administration of small doses of vitamins D, C, B_1 and B_2. Diathermy has not been observed to produce any undesirable side effects.

One of the most important affections in rickets is that of the muscular apparatus. This symptom is constant in all forms and at all periods of the rachitic process. It is particularly clearly marked in children with nutritional disorders. Treatment with vitamin D and other agents (ultraviolet irradiation, water, sun and light-and-air baths) often fail to produce positive results with respect to the muscular system, the treated children long retaining hypotonia and abnormal joint mobility.

A number of scientific studies now suggest that massage and physical exercise are very valuable therapeutic aids in the treatment of rachitic children with marked muscular hypotonia.

The value of movement for the normal growth and development of infants was discussed by N. M. Ambodik, Russian physician, who wrote as early as the end of the 18th century: "Insufficient bodily movement is the principal cause of the infant's slow growth", and "immobility inflicts great harm on anybody, especially on infants. A body that does not move is like standing water which grows mouldy, spoils and stagnates."

A. I. Polunin, outstanding physician of the middle of last century, in his article "Contribution to the Initial Education of Man" published in the *Moscow Medical Journal* in 1851 advised "strengthening the body with physical exercise when educating children" and emphasised that "physical exercise not only develops and strengthens the body and prevents disease, but also cures disease" (quoted from Y. D. Zabludovskaya).

The principal factor of the physiological effect of massage is the intensified flow of tissue fluids (lymph and blood) and, consequently, improvement in nutrition and all metabolic processes of the tissues. Systematic massage increases the size, strength and contractility of the muscles.

Massage must be combined with physical exercise. These two therapeutic factors are closely interconnected and supplement one another. The main aim of this form of treatment is to keep all the systems and organs of the child's organism as active as possible.

The K. M. Bykov school has demonstrated that the functions of all organs and systems are subject to the laws of conditioned reflex activity. Since most reactions are manifested in the form of movements, muscular activity, the latter is, as a rule, a conditioned stimulus. Forced immobility of the organism leads to weakening of the conditioned reflex connections and disturbances in the coordina-

tions of all systems and organs, which diminishes the biological activity of the organism.

The essential effect of massage and physical exercise consists in increasing the muscle tone, improving the processes of blood circulation, respiration, gas exchange and metabolism, and in perfecting the coordinating and regulatory mechanisms. It is believed that, as a result of mechanical stimulation of the skin during massage, the cell elements are destroyed and products of disintegration of the proteins of these cells are formed (among them—histaminic substances). On being absorbed by the capillaries and entering the general blood stream they act like foreign proteins. It has, moreover, been demonstrated that mechanical stimulation of the sensory nerve endings in the skin reflexly influences the functions of a number of organs and systems. During massage mechanical stimulation affects the vascular system of the organism—lymphatic, arterial and venous, as a result of which the blood and lymph circulation improves and venous stasis is eliminated. This stimulates increased consumption of oxygen by the tissues and enhances the oxidative and reductive processes of the organism (Y. D. Zabludovskaya, E. V. Salistovskaya). Massage and physical exercise are particularly important for rickets since it is well known that in this disease metabolism is impeded, the oxidative processes in the organism are weakened, unoxidised products of intermediate metabolism accumulate in the tissues, and the acid-base balance shifts in the direction of acidosis.

Massage improves the rachitic children's general condition, makes them livelier and more active, increases their appetite, intensifies their digestive processes, and the children begin to gain weight. According to some observations, systematic massage and physical exercise enable 3-9-months-old normally nourished children to gain an average of 600 g a month and undernourished children of the same age—700 g a month. Massage also effects an improvement of the motor functions.

The development of motor skills plays an important part in the child's general condition. For young children movements are a source of joy, good emotional tone, normal general development and proper functioning of all systems and organs. With good emotional tone all the biological processes in the organism operate more intensely and efficiently.

Massage and physical exercise are particularly important for undernourished rachitic children. The turgor vitalis and muscle tone of these children are very low and the children lag in the development of their static and motor functions. Low emotional tone and slow reaction to the surroundings are characteristic of children in this condition.

Massage and physical exercise increase the resistance of the child's organism, especially the respiratory tract to disease. With prolonged repetition of suitable exercises for the respiratory muscles the respiratory excursions become longer, the chest expands, intrathoracic pressure diminishes and the respiratory capacity of the lungs increases. All these factors enhance the resistance of the organism to bronchial and pulmonary diseases.

Systematic massage and physical exercise are very important for children in closed children's institutions (children's homes, sanatoriums for very young children) and in nurseries. For these children massage and physical exercise constitute not only stimulatory therapy in rickets and dystrophy, but also an agent for controlling hospitalism.

Massage, physical exercise and contact with an adult give the child great pleasure and joy, and favourably affect the central nervous system. The stimulating effect of the afore-mentioned physiotherapeutic measures on the vegetative nervous system is also important because the latter likewise plays an important part in the pathogenesis of rickets. This stands to reason if we consider the enormous role played by the trophic function of the nervous system in the biochemical processes of the tissues and cells of the

organism under the regulating influence of the cerebral cortex.

At the height of severe forms of rickets corrective exercise must be conducted very cautiously because it may evoke a negative reaction in the child owing to the pains in the muscles and bones, and may lead to infractions and fractures of the bones of the limbs. Very important at this period is effleurage. Massage is indicated at all periods of the disease because of its salutary effect on hypotrophy. Special attention must be devoted to massaging the legs and feet because of the impaired development of the static and motor functions of rachitic children. Owing to this, all exercises must first be formed in a recumbent position and only as the muscular system and ligamentous apparatus grow stronger may the exercises gradually be made more complicated and be performed in a sitting and then an upright posture.

During the period of convalescence corrective exercise must begin very cautiously, avoiding movements which may aggravate the deformities or sprain the ligaments.

Since rachitic children tire very easily and their nervous system is affected by the disease, it is necessary to limit the number of repetitions of each exercise and restrict each workout to 10-15 minutes.

Well elaborated sets of corrective exercises and massage are available. These sets have been compiled for two groups of children—debilitated and somewhat stronger. The exercises, forms of massage, their dosage and sequence have been worked out in accordance with the requirements of each of the two groups. Each set is calculated for 7-10 days of treatment. A total of 6 sets of exercises gradually growing more complicated must be employed in a course of treatment.

Climatotherapy and sanatorium treatment produce very good results. Changing the climate for very young children is not recommended for it may cause loss of appetite, emaciation and gastrointestinal disorders.

MODEL SETS OF CORRECTIVE EXERCISES AND MASSAGE FOR RACHITIC (HYPOTROPHIC) CHILDREN FROM 2-3 MONTHS TO 18 MONTHS OF AGE (FROM R. T. SOROCHEK)

Set 1

(for the first 7-10 days of treatment)

Sequence	Exercises	Number of repetitions	Sequence	Exercises	Number of repetitions
	Weak Group			*Stronger Group*	
	In the beginning of the session the child is placed prone with a sand role under the chest		1	General massage (effleurage, petrissage, circular rubbing, slapping) for 5-6 minutes	
			2	Circular arm movements	4-6
1	Effleurage for 3-4 minutes		3	Turning the child over by the legs from a supine to a prone position	2
2	Flexion and extension of the arms in the elbows	3-5	4	Imitation of swimmer's movements	1
3	Alternate flexion and extension of the legs	3-5	5	Simultaneous and alternate flexion and extension of the legs	4-6
4	Kicking in a prone position (if the plantar reflex is normal)	2-3	6	Crawling with outside aid	2-3
5	Passive adduction and abduction of the arms	3-5	7	Sitting the child up with both arms abducted	2
Total duration of the workout is from 8 to 10 minutes, including			8	Massage and exercise for the feet	4-6

(Continued)

Sequence	Exercises	Number of repetitions	Sequence	Exercises	Number of repetitions
	Weak Group			*Stronger Group*	
	the 2-4 minutes of lying in a prone position		9	Imitation bycicle riding	10-12
			10	Raising the body from prone position (by holding the child under the elbows) to a kneeling or upright position	2-3
			11	Passive adduction and abduction of the arms	4-6
			12	Imitation dancing	

Total duration of the workout is 12-13 minutes

Set 2*

1	General massage (effleurage and rubbing) 4-5 minutes		1	General massage (5-6 minutes)	
2	Flexion and extension of the arms in the elbows	3-5	2	Raising and lowering extended arms	3-4
3	Extending the spine lying on a side	2	3	Raising extended legs to a right angle with the body (if not contraindicated)	3-4
4	Kicking in a prone position (if the plantar reflex is normal)	3-4	4	Massage and exercises for the feet	4-6
5	Passive adduction and abduction of the arms	3-5	5	Imitation bicycle riding	10-12
6	Simultaneous and alternate flexion and ex-		6	Sitting the child up with both arms abducted	2
			7	Crawling (active)	3-4

* This and all following sets of exercises are calculated for 7-10 days and must be used only after the child has mastered the preceding set.

(Continued)

Sequence	Exercises	Number of repetitions
	Weak Group	
	tension of the legs in a supine position	4-6
	Total duration of the workout is 8-9 minutes	
	Note: The child must be placed in a prone position 3-4 times a day for 5-7 minutes each time during the waking hours	

Sequence	Exercises	Number of repetitions
	Stronger Group	
8	Alternate flexion and extension of the arms in a supine position	4-6
9	Turning the child by the legs from a supine to a prone position	2
10	Drawing the shoulders back forcefully, trying to make the shoulder-blades touch (in prone position)	2
11	Raising the body to an upright position (with support under the elbows)	2-3
12	Circular arm movements	5-6
13	Striding with support under the armpits	4-6 steps
	Total duration of the workout is 12-13 minutes	

Set 3

Sequence	Exercises	Number of repetitions
1	Massage (effleurage, petrissage) 4-5 minutes	
2	Raising and lowering extended arms	2-3
3	Extending the spine lying on a side	2
4	Kicking in a supine position with the legs encountering light resistance	4-6
5	Turning from supine to prone position	1-2

Sequence	Exercises	Number of repetitions
1	General massage—5 minutes	
2	Circular arm movements	3-4
3	Raising extended legs to a right angle with the body (if not contraindicated)	4-6
4	Sitting up by pulling with both abducted arms	2-3
5	Turning the child by	

(Continued)

Sequence	Exercises	Number of repetitions	Sequence	Exercises	Number of repetitions
	Weak Group			*Stronger Group*	
6	Passive adduction and abduction of the arms	4-6		the legs from a supine to a prone position	2
7	Imitation bicycle riding	10-12	6	Raising the body from a prone to an upright position	2
8	Massage and exercises for the feet	4-6	7	Crawling	3-4
			8	Adduction and abduction of the arms	5-7
			9	Massage and exercises for the feet	4-6
			10	Imitation bicycle riding	11-12
			11	Sitting the child up by pulling at the arms	2
			12	Walking, supported under the armpits	6-8 steps

Total duration of the workout is 8-10 minutes

Note: The child must be placed in a prone position 3-4 times a day for 10-12 minutes each time during waking hours

Total duration of the workout is 12-14 minutes

Set 4

1	General massage for 5-6 minutes		1	General massage for 5 minutes	
2	Passive standing	1	2	Adduction and abduction of the arms	5-6
3	Raising and lowering extended arms	2-3	3	Sitting up with both arms abducted	2-3
4	Turning from a supine to a prone position	1-2	4	Raising the child from a prone to an upright position with support under the elbows	2
5	Massage and exercises for the feet	4-6	5	Imitation bicycle riding	12-14
6	Crawling with outside aid (provided the child turns over on the belly unaided)	2-3			

(Continued)

Sequence	Exercises	Number of repetitions
	Weak Group	
7	Passive adduction and abduction of the arms	4-6
8	Imitation bicycle riding	8-10
9	Passive standing	1

Total duration of the workout is 10-12 minutes

Subsequently, the turn from a supine to a prone position is performed as an exercise

Note: If the child cannot as yet turn to a prone position unaided, it must be placed in a prone position for 12-15 minutes several times a day during waking hours

Sequence	Exercises	Number of repetitions
	Stronger Group	
6	Crawling on all fours (after a toy)	
7	Circular arm movements	4-6
8	Standing up from a sitting position with pressure applied to the outside borders of the feet	2-3
9	Walking, held by the arms	6-8 steps
10	Raising extended arms (inhalation) and lowering (exhalation)	3-4

Total duration of the workout is 12-14 minutes

Set 5

1	General massage (effleurage, rubbing, petrissage, circular rubbing) for 5-6 minutes	
2	Passive standing for 20-30 seconds	1
3	Adduction and abduction of the arms in a supine position	3-4
4	Sitting up from a supine position with both arms abducted, providing the child can raise the head and shoulder girdle unaided	2

1	General massage for 4 minutes	
2	Circular arm movements	4-6
3	Pulling up to a sitting position with the arms flexed in the elbows (provided the flexors contract actively)	2
4	Crawling on all fours (after a toy)	
5	Massage and exercises for the feet	
6	Imitation bicycle riding	4-6

(Continued)

Sequence	Exercises	Number of repetitions	Sequence	Exercises	Number of repetitions
	Weak Group			*Stronger Group*	
5	Crawling with outside aid	2-3	7	Abduction of extended arms and their slow adduction with a slap, the child sitting with the back towards the instructor	3-4
6	Raising the shoulder girdle and chest with support under the elbows in a prone position	2	8	Standing and first steps with adult aid	
7	Circular arm movements	4-5	9	Walking on the floor, supported by the arms	
8	Massage and exercises for the feet	4-6			
9	Imitation bicycle riding	10-12		Total duration of the workout is 12-14 minutes	
10	Passive standing for 20-30 seconds				
	Tot l duration of the workout is 10-12 minutes				

Set 6

1	General massage for 5-6 minutes		1	General massage for 4 minutes	
2	Circular arm movements	4-6	2	Circular arm movements	4-6
3	Pulling up to a sitting position with arms abducted (child making an active effort)	2-3	3	Massage and exercises for the feet	4-6
4	Raising extended legs to a right angle with the body (if not contraindicated)	3-4	4	Imitation bicycle riding	15-20
5	Rising to a kneeling or upright position,		5	Crawling on all fours	
			6	Rising from a prone to an upright position,	

(Continued)

Sequence	Exercises	Number of repetitions
	Weak Group	
	supported under the elbows (from prone position)	2-3
6	Crawling with outside aid	2-3
7	Passive adduction and abduction of the arms	4-6
8	Abduction of the shoulders until the shoulder-blades touch, in a prone position	2-3
9	Massage and exercises for the feet (flexion and extension, adduction and abduction)	4-6
10	Imitation bicycle riding	10-12
	Total duration of the workout is 11-13 minutes	
	Stronger Group	
	supported under the elbows	2
7	Bending and straightening the body with pelvis, knees and abdomen fixed (the child in a vertical position with back to the instructor)	2
8	Sitting up while being held by both arms	3-4
9	Alternate raising and lowering of each arm (in a supine position)	4-6
10	Walking in back of a wheel-chair (aided or unaided)	
	Total duration of the workout is 13-15 minutes	

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